NEUROCOGNITION AND DISABILITY IN PATIENTS WITH SCHIZOPHRENIA COMPARED WITH HEALTHY CONTROLS

Dissertation submitted by

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In partial fulfillment of the regulations required for the degree of

DOCTOR OF MEDICINE IN PSYCHIATRY

Under the guidance of

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PSG INSTITUTE OF MEDICAL SCIENCES AND RESEARCH

COIMBATORE

MAY – 2019

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled "**Neurocognition and Disability in patients with Schizophrenia compared with healthy controls"** is a bonafide and genuine research work carried by me under the guidance of Dr. I. Anand, Professor in the Department of Psychiatry, PSGIMS & R, Coimbatore.

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To
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Ref: Project No.17/154

Date: June 16, 2017

Dear Dr Sheerin Fathima,

Institutional Human Ethics Committee, PSG IMS&R reviewed and discussed your application dated 25.04.2017 to conduct the research study entitled "*Neurocognition and disability in patients with Schizophrenia compared with healthy controls*" during the IHEC meeting held on 05.05.2017.

The following documents were reviewed and approved:

1. Project submission form
2. Study protocol (Version 1 dated 25.04.2017)
3. Informed consent forms (Version 1 dated 25.04.2017)
4. Data collection tool (Versin 1 dated 25.04.2017)
5. Current CVs of Principal investigator, Co-investigator
6. Budget

The following members of the Institutional Human Ethics Committee (IHEC) were present at the meeting held on 05.05.2017 at IHEC Secretariat, PSG IMS & R between 10.00 am and 11.00 am:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Mr R Nandakumar (Chairperson, IHEC)	BA., BL	Legal Expert	Male	No	Yes
2	Dr. S. Bhuvaneshwari (Member-Secretary, IHEC)	MD	Clinical Pharmacology	Female	Yes	Yes
3	Dr S Shanthakumari	MD	Pathology, Ethicist	Female	Yes	Yes
4	Dr Sudha Ramalingam	MD	Epidemiologist, Ethicist Alt. member-Secretary	Female	Yes	Yes
5	Dr D Vijaya	M Sc., Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes

The study is approved in its presented form. The decision was arrived at through consensus. Neither PI nor any of proposed study team members were present during the decision making of the IHEC. The IHEC functions in accordance with the ICH-GCP/ICMR/Schedule Y guidelines. The approval is valid until one year from the date of sanction. You may make a written request for renewal / extension of the validity, along with the submission of status report as decided by the IHEC.

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Following points must be noted:

1. IHEC should be informed of the date of initiation of the study
2. Status report of the study should be submitted to the IHEC every 12 months
3. PI and other investigators should co-operate fully with IHEC, who will monitor the trial from time to time
4. At the time of PI's retirement/intention to leave the institute, study responsibility should be transferred to a colleague after obtaining clearance from HOD, Status report, including accounts details should be submitted to IHEC and extramural sponsors
5. In case of any new information or any SAE, which could affect any study, must be informed to IHEC and sponsors. The PI should report SAEs occurred for IHEC approved studies within 7 days of the occurrence of the SAE. If the SAE is 'Death', the IHEC Secretariat will receive the SAE reporting form within 24 hours of the occurrence
6. In the event of any protocol amendments, IHEC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. Alteration in the budgetary status should be clearly indicated and the revised budget form should be submitted
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval
   d. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented
   e. If there are any amendments in the trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IHEC and only then can they be implemented
   f. Any deviation-Violation/waiver in the protocol must be informed to the IHEC within the stipulated period for review
7. Final report along with summary of findings and presentations/publications if any on closure of the study should be submitted to IHEC

Kindly note this approval is subject to ratification in the forthcoming full board review meeting of the IHEC.

Thanking You,

Yours Sincerely,

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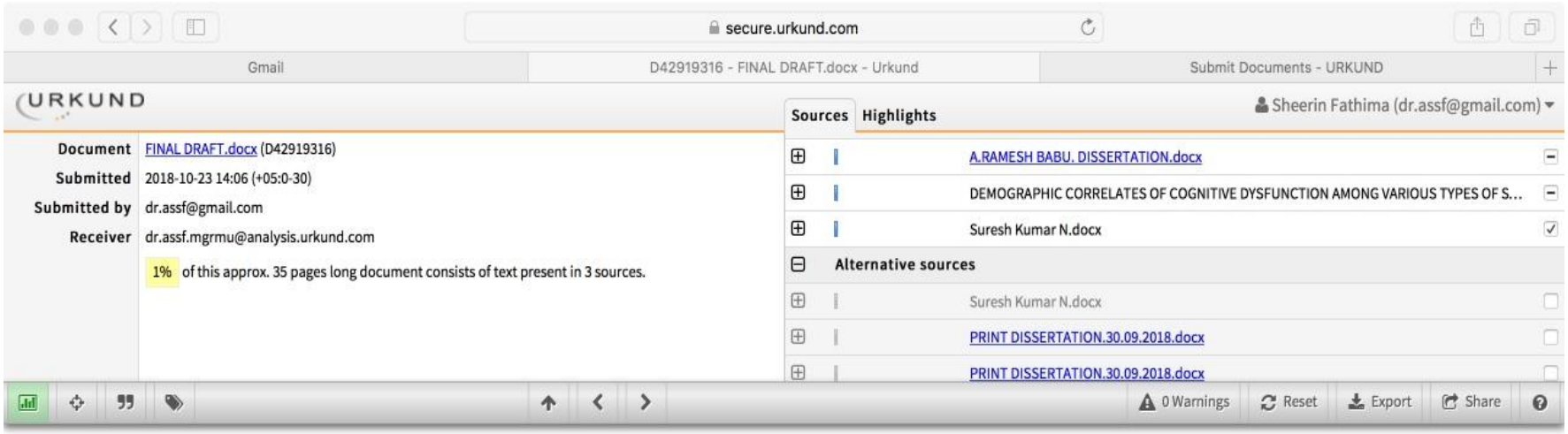
Dr S Bhuvaneshwari
Member - Secretary
Institutional Human Ethics Committee



NEUROCOGNITION AND DISABILITY IN PATIENTS WITH SCHIZOPHRENIA COMPARED WITH HEALTHY CONTROLS

ABSTRACT

Dr.Sheerin Fathima A S, Postgraduate in Department of Psychiatry, PSGIMSR

BACKGROUND: Majority of patients with schizophrenia have life-long disability in their social and occupational functioning. Cognitive impairment is recognized as an important domain of schizophrenia, with a wide range of deficits seen among patients with schizophrenia.

AIM: The current study aimed at assessing the neurocognitive function in clinically stable schizophrenia patients, in comparison with age and gender matched controls. Secondary aim was to assess any correlation between neurocognitive deficits and duration of illness ; neurocognitive deficits and disability among patients with schizophrenia.

METHODOLOGY: 20 clinically stable schizophrenics & 20 age and gender matched healthy controls were included in the study. Select 8 tests from the NIMHANS Neuropsychological battery was used to assess the neurocognitive functions such as attention, processing speed, verbal learning and memory, executive functions, visual memory and visuo-spatial skills.

RESULTS: Results revealed a statistically significant difference between the two groups in the performance of all neurocognitive tests, with the schizophrenia patients group scoring lesser. Within

CERTIFICATE – II

This is to certify that this dissertation work titled "**Neurocognition and Disability in patients with Schizophrenia compared with healthy controls"** of the candidate **Dr. SHEERIN FATHIMA A. S.** with registration Number ..**201628303**..for the award of **M.D. degree** in the branch of…**PSYCHIATRY**… I personally verified the urkund.com website for thepurpose of plagiarism Check. I found that the uploaded thesis filecontains from introduction to conclusion pages and result shows. **1 %**…percentage of plagiarism in the dissertation.

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ABSTRACT

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RESULTS:

Results revealed a statistically significant difference between the two groups in the performance of all neurocognitive tests, with the schizophrenia patients group scoring lesser. Within the patient group, those with duration of illness < 2 years scored more on tasks for attention, verbal learning and memory and visual memory & had lower degree of disability, which were statistically significant.

CONCLUSION:

The current study emphasizes on the importance of assessing neurocognitive functions in all schizophrenia patients. Recently, cognitive remediation therapy is being done to improve the neurocognitive functioning which can have a significant implication on the overall well-being of the patient.

KEY WORDS: neurocognition, cognitive deficits, schizophrenia, disability, functional, neuropsychological

INTRODUCTION

Schizophrenia is a major mental illness posing a challenge to both who suffer from the disease as well as to those who are involved in treating the disease. It is considered to be one of the most puzzling diseases of the brain. Schizophrenia includes various domains of symptoms such as psychotic symptoms, deficits in cognitive functioning and significant psychosocial impairment. Schizophrenic disorders are characterized by fundamental and characteristic distortions of thinking and perception, and by inappropriate or blunted affect. Clear consciousness and intellectual capacity are usually maintained, although certain cognitive deficits may evolve in the course of time. The course of the disorder usually shows great variation and is by no means inevitably chronic or deteriorating.

Understanding the complex neural mechanisms that are involved in the disease process is essential for establishing the reason behind such widespread and significant impairment. It is also especially important to develop specific treatments such as drug targets or other therapeutic measures. The later years of 20^{th} century saw the rise of numerous antipsychotic medications that were developed to treat Schizophrenia. With the recent advancements in research, fundamental knowledge about the neural basis of the illness has been postulated. Studies are also being done on the possible genes involved, cellular or molecular mechanisms responsible for this disease. Thus, we can positively hope for new and advances treatment measures for this debilitating and deteriorating disorder.

An important development in the understanding of the psychopathology of schizophrenia is an appreciation of the importance of cognitive impairment in the disorder. Tremendous effort has gone into identifying the type and extent of impairments and its associated factors. The current diagnostic manuals such as ICD-11 or DSM-5 does not include neurocognitive deficits as a diagnostic criterion for Schizophrenia. But, DSM-5 has included extensive discussions about neurocognitive domain in schizophrenia. It is also suggested that, neurocognitive assessment should be considered as a part of routine clinical evaluation and should be universally done for each patient with schizophrenia. Although these impairments cannot function as diagnostic tools, they are strongly related to the functional outcome of the illness and, for that reason, have clinical value as prognostic variables, as well as for treatment planning. The cognitive impairments of schizophrenia have become the target of pharmacological and psychosocial treatment trials in the recent years. Despite the large number of research in this area in the last two decades, we still have to bridge the wide gap in the treatment of these cognitive impairments.

REVIEW OF LITERATURE

In the late nineteenth century, Emil Kraeplin described "Dementia Praecox", a major mental illness which he thought was a disease of the brain. In the early 20th century, Eugene Bleuler called the same illness as "Schizophrenia" which in Greek means "split mind". Bleuler also thought that the disease was due to brain pathology. Thus, the "cognitive" domain of the illness has been recognized since the earliest days in the history of schizophrenia.

Schizophrenia has always been considered an illness with life-long disability. The studies on outcome of schizophrenia has shown significant betterment with the advent of antipsychotics. The trend of outcome over a period of 100 years, from the late 19th century to late 20th century is such that, the individuals with schizophrenia having good outcome, has increased from 30% to 37%. (50)

Earlier, it was thought that the overall improvement was largely based on clinical symptomatology. But, over the last few decades, cognitive functioning has been established as predictor of quality of life and social/ occupational functioning, especially in the areas of ability to sustain employment, problem- solving skills that is necessary for daily living activities. Thus, the emphasis is currently on improving the quality of life, to improve the overall outcome of the illness. (30)

Over the years, the interest of the researchers into the neurocognition has seen many ups and downs. Since the birth of 21st century, this particular domain of schizophrenia is being studied intensely. (22)

DOMAINS OF DEFICITS IN NEUROCOGNITION

The assessment for neurocognitive functioning can be done using a wide range of tests which usually does not a test strictly one particular domain, rather one test can assess 2 or more domains. In schizophrenia, the most important domains of neurocognition are schizophrenia are working memory,attention/vigilance, verbal learning and memory, visual learning andmemory, reasoning and problem solving, speed of processing, and socialcognition.[44,46]

A meta-analysis done in 1998 by Heinrichs and Zakzanis, included 204 studies done worldwide from 1980-1997, to assess the neurocognitive performance of patients compared with controls. The studies included assess a wide range of cognitive functions such as Global and selective verbal memory, non-verbal memory, motor performance, attention, spatial ability, executive functions, language functions, tactile transfer and general intelligence. This meta-analysis found a prevalence rate of 61-78% neurocognitive deficits, which was more than that reported in previous studies. It also postulated that, neurocognitive deficits seen in schizophrenia can be on a continuum ranging from mild to profound deficits, rather than a cut-off range. It is also said that the cognitive functions of a particular patient depend on his premorbid level of functioning. Thus, the performance of schizophrenics with mild cognitive deficits may overlap with the performance of healthy controls, but still have dysfunction compared to his/her own potential. It was found that schizophrenics had neurocognitive deficits of large or moderate effect sizes on all the neurocognitive tests. [14]

The limitations of the study include, heterogeneity of the study population, use of a wide range of assessment tools in each study, inadequate recording of clinical and demographical variables. The argument of neurocognitive deficits being on a continuum, could mean that half of the schizophrenics may overlap with healthy control groups. Thus, assessing the premorbid level of functioning becomes more essential, which was not done in most of the studies due to various practical difficulties.

Another meta-analysis with similar study design, done by Raquelle et al (2010) included 47 studies with a total of 2,204 First episode Schizophrenia patients and 2,775 age and gender matched control groups. It analyzed 10 cognitive domains including language, motor skills, general cognitive ability and social cognition. Medium to large impairments were observed in all the cognitive domains, with maximal deficits seen in immediate verbal memory and processing speed. Similar to the previous meta-analysis, this study also put forth limitations such as limited information on moderator variables and significant heterogeneity across the studies. (17)

Various meta-analysesrevealed that, deficits in learning and memory and processing speed were of largest effect sizes, whereas deficits in other domains were of moderate to large effect sizes. Results from various methodologically sound studies showed that the deficits were in the range of 1 to 2 standard deviations below the healthy controls. (2)

Thus, in conclusion, severe impairment in verbal learning and memory is the most consistent finding across a large number of studies which is also seen to be fairly stable throughout the course of illness, with moderate deficits in almost all neurocognitive domains. [43]

LEARNING & MEMORY IN SCHIZOPHRENIA

It has been well established that verbal learning and memory is severely affected in schizophrenia and this deficit also remains relatively stable throughout one's life[17,13]. In the process of learning and memory, various complex neural networks are involved that are responsible for encoding and retrieval (recall) of information. In schizophrenia, both these processes are impaired, but performance relatively better on cued-recall. This suggests an involvement of Prefrontal cortex and medial temporal lobe, resulting in such deficits. The neurocognitive tests have shown that schizophrenia patients perform comparatively better on recognition tasks than on free-recall tasks. [20]

Knowledge corruption denotes holding false information with high belief, impaired cognitive insight and deficits in accepting the limited cognitive functioning. Patients with schizophrenia have been observed to have high knowledge corruption. It was also seen in a cross-sectional study on 71 patients that there is a significant positive correlation between impairment in verbal learning and memory and knowledge corruption in schizophrenia. Thus, impairment in verbal learning and memory can also affect one's ability to draw conclusions from the real-world experiences.[13]

Hence, as a result of defective verbal learning and memory, schizophrenia patients may show impairment in episodic memory, drawing faulty conclusions in real-life situations which could in turn, predict the functional outcome. [20]

ASSOCIATION WITH SOCIODEMOGRAPHIC VARIABLES

Various studies have been done to analyze the relationship between demographical variables such as age, gender, education, geographical region, and has given controversial reports.

In view of the differences in the neurotransmitter systems in the male and female brain, lot of studies have looked into the differences in the psychopathology, response to treatment and outcome in schizophrenia. With regards to the cognitive domain, studies analyzing the gender differences have showed inconsistent findings. Some studies have showed better performance on memory tasks in females, compared to males. Few other studies reported male schizophrenics have an overall better cognitive performance compared to females.[7] One of the major limitations in these studies were the tools used for assessment. With the advent of MCCB (The MATRICS Consensus Cognitive Battery), standardized tool developed by the NIMH, a study was done in 112 male schizophrenics and 80 female schizophrenics along with a control group. The study showed that females performed better on several cognitive domains with a moderate effect size, except in tasks for working memory & reasoning and problem solving. The study also showed that largest differences between males and females were observed in processing speed. It was also seen that

processing speed, verbal learning and memory and visual learning were independently associated with gender.[30]

The same study also showed that processing speed and verbal learning and memory were independently associated with age. [30]

A cross- sectional study was done in community dwelling individuals to study the relationship between age and cognitive deficits in schizophrenia. 235 schizophrenia patients in the age range of 19-79 and 333 healthy controls in the age range of 20-81 were included. It was found that the cognitive deficits in schizophrenia had a similar trajectory and rate of decline with ageing in all MCCB domains, except social cognition. The concludes by saying that schizophrenia can be considered as an illness with premature ageing wherein the cognitive deficits set in earlier in their lives, but remain stable without any accelerated decline in older age. This is contradictory to the studies that found an accelerated decline in the cognitive deficits when measured using other, non-MCCB assessment tools[8]. The study limitations included the cross-sectional study design and less number of subjects in age group older than 70.

A cross-sectional study done in 100 schizophrenia patients and 100 healthy controls among the Indian population revealed that older age was significantly associated with more decline in attention, memory and executive function, which is similar to the effect of ageing in the brain of a healthy individual. Among gender, male subjects had a poorer performance on memory tasks. Years of education was positively correlated with better performance on neurocognitive tests. [53]

Studies also found that, cognitive deficits were more and had rapidly declining trajectory in institutionalized individuals compared to community- dwelling individuals. The reasons for this could be, institutionalized individuals have more severe illness and community-dwelling individuals have a more stimulating environment leading to better cognition.[8,37]

Cognitive reserve is a concept developed to assess the ability of the diseased brain to use the cognitive networks in task performance. Over the years, cognitive reserve has been assessed with various indicators. Most commonly used indicators are premorbid IQ, years of education & occupation, leisure activities.[51,52]

A prospective, 2 years follow up study was done in 52 First episode schizophrenia subjects and 41 healthy age and gender matched controls. The study analyzed the relationship between cognitive reserve and neurocognitive functioning, which was measured using standardized neuropsychological tests. It was found that subjects with higher cognitive reserve was significantly associated with better scores on working memory, executive function, verbal memory and attention. In addition to that, it was also concluded that cognitive reserve mediated working memory and executive function at baseline and the working memory at 2 years follow-up.[3] This study gave an outline on how premorbid IQ and level of functioning can affect the neurocognitive functioning.

The level of education, especially formal education of more than 15 years, has been found to be an independent predictor of better cognitive performances in most of the

studies, although few studies have also given controversial results reporting no significant association between education and cognitive performance. In the studies showing a positive correlation between education and cognition, significant association is seen with various cognitive domains including social cognition.[7,26,30]

A recent meta-analysis (2013) of 100 studies done worldwide analyzed the differences in cognitive deficits based on geographical region. The results showed no significant differences based on the geographical region and deficits were fairly consistent among all regions. It also showed that cognitive deficits in males were of larger effect sizes compared to females, i.e., males with schizophrenia had more deficits in neurocognition.[2]

Thus, among the demographical variables, years of education and premorbid level of functioning was seen to be significantly associated with neurocognition in schizophrenia. In most of the studies, evidences regarding association with gender was controversial and inconclusive, although a recent extensive meta-analysis showed more deficits in males. The cognitive decline with age in schizophrenia resembled a similar pattern as seen in healthy individuals, thereby concluding that schizophrenia is an illness of premature ageing with relative stability after the onset of cognitive deficits.

COURSE OF NEUROCOGNITIVE DEFICITS

Since the advancements in research, there has been an on-going argument about schizophrenia being a neurodegenerative disorder or a neurodevelopmental disorder. Although, initially some neuroimaging studieshypothesized schizophrenia to be a neurodegenerative disease, in the recent years, other studies support the neurodevelopmental disease model, mainly owing to the stability of the cognitive deficits over time. In few studies, it was found that these cognitive deficits even improve over time.

A 5-year follow up study was done in 26 first episode psychosis patients and the course of cognitive functions such as executive functions, learning and memory, verbal fluency, attention, working memory, processing speed and abstract reasoning were analyzed. The neuropsychological tests were done twice – baseline at 6 months and follow up at 5 years. The study revealed that all neurocognitive domains except working memory and processing speed were seen to be significantly improved over time.[4] This means that, among the neurocognitive deficits, impairments in few domains seem to be stable over time while others improve. The results of this study, again support the neurodevelopmental model of schizophrenia.

A meta-analysis of 47 studies, analyzing the neurocognitive deficits in first episode schizophrenia, showed that larger deficits were seen in the general cognitive ability or

IQ in the first episode schizophrenics compared to the premorbid level. During the later stages of illness, the deficits seen were comparable with that of the first episode. Thus, significant deterioration from the premorbid level occurs even in the first episode which becomes relatively stable after that.[17]

A 6 month follow up prospective study in 82 first episode psychosis patients compared neurocognitive performance at baseline and after 6 months using CANTAB (Cambridge Neuropsychological Test Automated Battery). The study revealed that scores in working memory, processing speed and executive function seemed to improve over time. But, performance in verbal memory and spatial recognition seemed to have decreased significantly. [7]

Similar results were found in a 2 years follow-up study, which was a part of the multi follow up Oslo study, wherein 28 schizophrenia patients were compared with 28 healthy controls and was seen that, at 2 years follow-up assessment, there was a statistically significant decline in verbal learning and memory. Another interesting finding was that, the deficits in verbal learning and memory was greatest at the early phase of illness. It was also observed that there was an improvement in other neurocognitive domains at the 2-year follow up with significantly larger improvement in reasoning and problem solving and social cognition. [5]

A recent meta-analysis of 376 studies showed that there was no significant association between duration of illness and extent of cognitive deficits.[2] As discussed earlier, most of the studies show that, cognitive deficits tend to stabilize over time and does not vary with duration of the illness. [6,8,13,17]

A cross-sectional study of comparing 105 first-episode schizophrenia, 176 chronic schizophrenia and 300 healthy controls showed that, group with first episode schizophrenia had a significantly lesser deficit in working memory and social cognition compared to chronic schizophrenia group.[47]

A large, prospective, cohort study done in the Danish population wherein the schizophrenia patients were followed up for 10 years, showed that later age of onset predicted poorer performance on cognitive functions. [6] This is in contrast to the majority of the studies showing more cognitive deficits with early age of onset of illness. One explanation could be that, the mentioned study included participants with adulthood onset of illness, thereby having a potential limitation in the selection of participants.

A meta-analysis of 109 studies that analyzed the effect of age of onset on cognition, found that patients with earlier age of onset, especially onset at less than 19 years of age, was significantly associated larger deficits in almost all neurocognitive domains. [38] One major limitation of the study was that, it involved very less number of studies on late-onset schizophrenia, which could have potentially influenced the results.

Most of the studies has given robust evidences for decline in verbal learning and memory and working memory over time, with some evidences for decline in processing speed. The deficits in other neurocognitive domains remain relatively stable irrespective of the duration of illness. Studies also suggest that cognitive deficits are seen even as a part of the prodrome of schizophrenia. There is also evidence suggesting that intervention done early in the illness has a better outcome. Thus, it becomes important to identify people at ultra-high risk for schizophrenia, so that effective treatment for the cognitive impairment can be initiated in the prodrome itself. [34]

NEUROCOGNITION AND CLINICAL OUTCOME

A Systematic review of 13 studies done from 2002- 2012, by Lepage et al (2014) analyzed neurocognitive deficits in remitted Vs non-remitted patients. Most of the studies included revealed a significant trend of poorer performance on verbal learning and memory in non-remitted patients as well as in non-responders to neuroleptics. [1]

Although, few studies showed lower scores in visual memory, working memory, speed of processing among the non-remitted patients, majority of the studies failed to establish any significant association. [1]

Patients in the non-remitted group, obtained low scores in some of the tasks to assess reasoning and problem solving, although similar results were not seen in all studies. Thus, the association between problem solving skills and clinical improvement is controversial.[1]

This study concludes by saying that robust evidences are available for possible correlation between deficits in verbal learning and memory and poor clinical outcome. But, it does not rule out the association between deficits in other domains and clinical outcome. Rather, there may be association between specific neurocognitive tests and clinical outcome as seen with this systematic review study. Thus, future studies should use standardized neurocognitive batteries such as CogState Schizophrenia Battery or MATRICS Consensus Cognitive Battery. Though, most of the individual studies included in this review used definition for clinical remission given by Nancy Andreasen, few studies used other definitions. So, future studies should also consider assessing clinical remission using standard and consistent definitions. [1]

There is robust evidence for a significant association between negative symptoms and cognitive deficits in schizophrenia. A 3 year follow up study done in first episode psychosis patients, found that impairment in verbal memory, processing speed and executive functions was significantly associated with more severe negative symptoms which in turn leads to poorer clinical outcome (Addington et al.,2005).[13]

Another 5 years follow-up study, analyzed the association between deficits in neurocognitive domains and clinical outcome. It was found that deficits in working memory, particularly, was significantly correlated with negative symptoms. This working memory impairment was also seen to be stable over time, thus could result in long-standing residual negative symptoms. This study did not find any significant association between positive symptoms and neurocognitive deficits. [4]

Another study done in Indian population on first episode psychosis patients, found that giving cognitive retraining program significantly improved executive functioning which in turn improved the negative symptoms. [28]

A 6 months follow-up study in first episode psychosis patients showed that, compared to baseline, executive functioning had significantly improved which was positively correlated with clinical improvement, measured with BPRS scale.[7]

Hence, evidences supporting the association of cognitive domains, such as verbal learning and memory, executive functioning with the negative symptoms of schizophrenia are available in abundance, and improving these deficits should be an integral focus in the treatment of schizophrenia.

NEUROCOGNITION AND FUNCTIONAL OUTCOME

Neurocognition is defined by the cognitive skills involved in carrying out psychological processes, and can be divided into independent but interrelated subdomains. Intact neurocognition is essential for social functioning [13,14].

Functional outcome involves functioning in various areas such as self-care, independent living, interpersonal relations, community activities and employment. (1)

Lepage et al., (2014) noted that impairment in cognitive functioning is highly correlated with poor self-care and predicts poorer performance in daily routine activities. This finding still needs to be studied further. (1)

Independent living is another variable in functional outcome that is seen to be correlated with functioning in cognitive domains, especially verbal memory. Poorer verbal memory performance predicts a significant impairment in independent living ability, which in turn is seen to be negatively correlated with clinical outcome i.e., remission of psychotic symptoms. (1)

A randomized controlled study, done by Caplan et al., 2008, studied 2 groups of clinically stable homeless schizophrenics, who were randomly assigned to group residence or independent apartments. It concluded that clinically stable schizophrenia patients who were moved to a group residence, not only had better clinical outcome,

but also showed improvement in their performance on tasks of attention and verbal memory. [49]

Deficits in neurocognitive functioning is seen to be only minimally associated with social and interpersonal functioning, although social cognition is a robust predictor impairment in social functions. [1]

Deficits in cognitive functions is found to be negatively correlated with community activities and participation. This may be due to various limitations put forth by the cognitive deficits. Limited executive functioning, which could lead to poor planning, impaired shopping skills, poor navigation abilities, poor driving skills results in deficits in everyday living skills and participation in the community. This is even more restricted, due to the financial constraints and being forced to live in an unfriendly neighborhood. [1,51,52]

A 2 years follow-up, prospective study which was done as a part of multi follow-up Oslo study, found that there was no significant association between verbal memory and functional outcome, measured in terms of social and role function items on Global Function scale. There was a positive correlation of the cognitive domains of attention/ vigilance and reasoning & problem solving with social and role functioning.

A cross-sectional study analyzing the effect of various cognitive domains in real-world behavior revealed that domains such as attention and working memory is directly associated with work skills, whereas executive functions was associated with

interpersonal skills. Processing speed was seen to be significantly related to both social and occupational competence.[18]

Among the various domains of neurocognitive deficits, a 5 year follow up study in first episode psychosis subjects, found a significant association between working memory deficits and functional outcome as measured by FAST (Functional Assessment Short Test)[4]. This study also suggests that, this poor functional outcome may be due to the negative symptoms of schizophrenia, which were also significantly associated with working memory deficits.

A meta-analysis of 20 studies studied the relationship of neurocognitive domains with subjective measures of Quality Of Life (QOL) and objective measures of Quality Of Life. It showed that all neurocognitive domains were positively correlated with objective QOL. In contrary, almost all neurocognitive domains were either not significantly associated or negatively correlated with subjective QOL. Only verbal fluency was positively correlate with subjective QOL. This study emphasizes on the significant differences in the association of neurocognition and subjective/ objective measures of QOL and thereby the need to address the same in treatment implications.

Thus, the most important predictors of functional outcome are attention, verbal learning and memory and executive function. Social cognition is strongly associated with social/ community functioning.

GENETICS OF NEUROCOGNITION IN SCHIZOPHRENIA

Recently, various researches are done to study the relationship between neuro-biological markers or genetic loading and neurocognition in schizophrenia. This has also given rise to arguments that neurocognitive impairment should be considered as a genotype/ endophenotype in schizophrenia.

Studies have established that neurocognitive deficits in schizophrenia are highly heritable. But, among the various domains of deficits, which domains are affected due to genetic loading is still under research. Few studies have showed that first degree relatives of schizophrenia patients have deficits in neurocognitive functioning with a small to medium effect size. Of these, deficits in IQ and working memory are found to be highly due to genetic loading.

A cross –sectional study done on 28 patients and 129 unaffected biological parents compared the neurocognitive deficits with matched control group. It was found that both the unaffected parents of a schizophrenia patient showed medium effect sized deficits in attention, memory and executive function. Among the unaffected parents, the most likely carriers showed larger impairment in attention and executive function, thereby supporting the role of genetic loading in the deficits. [(24)]

An Indian study of a small sample size analyzed the neurocognitive functioning of schizophrenia patients, compared with their unaffected siblings and healthy controls. The unaffected siblings were noted to perform poorly on verbal learning and memory compared to healthy controls. Although, this study showed significant difference in

only verbal learning and memory, various other studies have found that the unaffected siblings show impairments also in other domains such as working memory and executive functions with modest effect sizes. [25]

Another Indian Study analyzed the relationship between P300 and neurocognition in patients and unaffected siblings compared to healthy controls. It was found that, both P300 and neurocognitive deficits fall on a continuum, wherein the healthy controls are on an extreme, schizophrenia patients on another extreme with the unaffected biological relatives occupying an intermediate position.[54]

Oxidative stress is postulated as a cause in many psychiatric disorders; most of the studies have found oxidative stress to be associated especially with Schizophrenia. Oxidative stress markers such as Glutathione(GSH), Nitric oxide(NO), Superoxide dismutase(SOD), Glutathione peroxidase, BDNF, Neurotropin 4/5 (NT4/5) are some examples of the biomarkers that are being extensively studied. A large number of studies have found a positive correlation between oxidative stress biomarkers and neurocognitive deficits; evidences are coming up for association with high levels of Malondialdehyde, Nitric oxide and low levels of Glutathione, Superoxide dismutase. Martinez-Cengotitabengoa and colleagues were the first to investigate the potential relationship between the levels of oxidative stress and neurocognition in schizophrenia, and found a significant correlation between GSH and executive function.

Gonzalez-Liencres et al., in 2014, studied the association of oxidative stress biomarkers with neurocognition and social cognition in 50 clinically stable schizophrenia patients. They found a statistically significant positive correlation between NT4/5 levels and executive function and visual attention. Interestingly, no significant correlation of biomarkers was found with social cognition.[16]

Thus, from the available research, one can say that due to genetic loading, there is an innate vulnerability to develop schizophrenia and when environmental factors exploit that vulnerability, the illness sets in.

ASSESSMENT TOOLS

One of the major limitation in the studies on neurocognition in schizophrenia is the use of a long list various assessment tools, which makes comparisons between individual studies difficult. The tools can be an extensive list of tasks testing various domains, multiple tasks testing one or two specific inter-related domains, composite tool with a few important tasks to assess the general neurocognitive functioning. The choice of an assessment tool should be based on the purpose of the study. For clinician's use, an easily administered tool that is less time consuming should be preferred, such as SCoRS, UPSA, RBANS, BACS, BCA. Among these, UPSA, SCoRS and BCA also assess the functional outcome. For research purposes, extensive batteries like WAIS, WMS, MCCB can be used. In many studies done in the past, RBANS, BACS, WAIS, WMS, a list of specific tasks to assess the specific domain

have been used. Recently, NIMH funded MATRICS initiative has come up with MCCB, which is the most commonly used tool in the recent years of research. [35]

[SCoRS = Scale for Cognition in Schizophrenia; UPSA = University of California Performance-Based Skills Assessment; RBANS = Repeatable Battery for Assessment of Neuropsychological Status ; BACS = Brief Assessment of Cognition in Schizophrenia ; BCA = Brief Cognitive Assessment ; WAIS = Wechsler Adult Intelligence Scale ; WMS = Wechsler Memory Scale ; MCCB = MATRICS Consensus Cognitive Battery]

IMPLICATIONS IN TREATMENT

Traditionally, schizophrenia is treated with antipsychotic medications and it has been well established that, it significantly improves the clinical outcome. When the cognitive deficits are considered, the role of antipsychotic treatment is yet to be explored. Studies have found that, both, patients with antipsychotic treatment history and drug naïve patients, displayed similar profile of neurocognitive deficits, which suggest that, antipsychotics may not improve the cognitive deficits. [43]

The CATIE trial, which is a double blind, randomized controlled trial, analyzed the neurocognition in 817 patients, who were randomized to 4 second generation antipsychotics such as risperidone, olanzapine, quetiapine, ziprasidone and first generation antipsychotic Perphenazine. At 2 months following treatment, minimal

improvement in cognitive deficits were noted, with no statistically significant difference between the drugs. But, the study showed only a negligible effect size and also had significant biases. [48]

Most of the studies analyzing the effect of second generation antipsychotic treatment on cognition showed only small effect sizes, and also had lot of methodological issues. [43] Studies comparing first generation and second generation antipsychotic medications, were mostly either funded by sponsor with a conflict of interest, or used inappropriate doses of drugs to compare. One thought to be considered while choosing antipsychotic medications is that, first generation antipsychotics, due to its high propensity for extra pyramidal side effects, will most often require an anticholinergic drug, which can worsen the cognitive impairment. [43]

A randomized double blinded placebo-controlled, phase II study was done in chronic schizophrenia patients wherein, the effect of Recombinant Human Erythropoietin was analyzed on cognition, based on the evidence on neurotrophic effects of rhEPO. The neurocognitive functions were assessed at various points of time over 12 weeks. The study showed that both rhEPO group and placebo group showed some improvement in all cognitive domains with a slightly more, statistically significant improvement in the rhEPO group, which was independent of the effect on other symptom domains of schizophrenia. But, the study had limitations such as, the sample size was very small, duration of treatment was only 3 months, and the effect sizes were also small. [10]

There is preliminary evidence suggesting the beneficial effects of adjuvant estrogen in improving the cognitive functions in schizophrenia, especially verbal memory. This is based on the concept and evidence that estrogen in the brain promotes neuronal growth and neuronal plasticity thereby acting as a neuroprotective agent. But, due to the risk of various adverse effects in the long-term use of estrogen, this area is still under-explored. A double blinded, placebo controlled RCT done over 13 weeks with a cross-over study design, analyzed the effect of adjuvant Raloxifene, which is a selective second-generation estrogen receptor modulator when given for 13 weeks. The results showed significant improvement in attention and processing speed at 13th week in the Raloxifene group. But, the study was not devoid of limitations, in its study design, selection of patients and the short duration of treatment. [36]

There is a large number of studies published in the recent years, supporting the use of glutamatergic agents after the piling evidence for glutamate hypothesis in schizophrenia. Drugs acting on NMDAR, which are currently in phase II or III trials include Glycine site agonists such as Glycine and D-serine, Glycine reuptake inhibitors like bitopertin, Metabotropic type 5 receptor agonists, α 7 nicotinic agonists. But, the largest of the effect sizes from these studies were only 0.3, which is a small effect size statistically. Other drugs that target 5HT-A1 and 5HT-A7 (Lurasidone) which are serotonergic receptors are also being studied, but with inconclusive evidences supporting these. Cognitive enhancers such as Donepezil or Modafinil are not found to be useful. [55]

There have been many studies done in the western countries looking at the effect of cognitive retraining or cognitive remediation therapy on the cognitive deficits seen on schizophrenia, targeting specific neurocognitive domains. The studies revealed mixed results with few studies showing positive results including improvement in cognitive deficits, negative symptoms and thereby improving the functional outcome. It was also seen that cognitive retraining given in the early phase of illness gave more benefits. Multiple meta-analyses done in this area showed robust evidences with a medium effect size supporting cognitive retraining [(55)]. But, there were lot of limitations in putting it to practice, which included high cost of treatment, frequent hospital visits and thus, resulting in poor adherence to therapy. It was also seen that, though some improvement was seen in the neurocognitive tests, it was not consistently correlated with improvement in functional outcome i.e., the improvement in the neurocognitive tests were not translated to improvement in social/ occupational functions in real life.

In Indian set-up, the high cost of treatment and limited availability of training personnel, becomes very important factors that limits the adherence and effective delivery of cognitive remediation therapy. Thus, home-based cognitive retraining programs started gaining popularity. A randomized controlled study to examine the effectiveness of the same, was done in 45 first episode psychosis patients, where patients were randomized to treatment as usual group and adjuvant cognitive remediation training. The training was delivered under the supervision of a care-giver daily at home for 2 months and the tasks were graded based on difficulty. At the end of 2 months, the cognitive retraining group showed significant improvement in

executive functions such as divided attention, planning, concept formation and set-shifting ability, which sustained till 6 months. The study had some serious limitations, small sample size, significant drop out, no blinding for the rater for assessment. [28]

Although lot of research has been done on treatment for neurocognitive dysfunction, no conclusive evidence has come up for any of the treatment modalities. Thus, NIMH sponsored an initiative to bring the researchers, clinicians, Pharmaceutical companies together to develop standardized tools to assess and drug targets that would improve cognition in schizophrenia. MATRICS – Measurement and Treatment Research to Improve Cognition in Schizophrenia was the first in that initiative which came up the standardized tool MCCB (The MATRICS Consensus Cognitive Battery) assessing 7 neurocognitive domains that are to be the main focus in schizophrenia[44]. Due to certain limitations in MATRICS, another initiative was developed – CNTRICS i.e., The Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia [46]. In the recent years, CNTRICS has been conducting meetings and research in developing imaging biomarkers, such as, fMRI, EEG, EMG and TMS which can be used in identifying targets and drug developments. [23,46]

Currently, we stand at a place where we don't have conclusive evidence supporting pharmacotherapy for neurocognitive dysfunction seen in schizophrenia. Cognitive remediation, especially when given in the early phase of illness, appears to have enough evidence to support its use, but it comes with a lot of limitations too.

RATIONALE FOR THE STUDY

With the up-roar in the neurocognition in schizophrenia in the recent year, many studies have been done worldwide regarding the cognitive deficits and functional outcome in schizophrenia. As we all know, the overall outcome of schizophrenia in developing countries like India is not the same as that of western countries. To our knowledge, there are no Indian studies that directly correlates thecognitive deficits with the disability in schizophrenia among Indian population. And the few studies on cognitive deficits among the Indian population have used tools that are developed in the western countries, which may have cultural variations and makes it difficult to use those tools without modifications. Thus, studies looking into both neurocognition and the functional outcome in our population using validated tools specifically developed in our cultural context may render a better knowledge regarding cognitive deficits and disability in the Indian schizophrenia patients.

AIM

To assess the neurocognitive functions among patients with schizophrenia and compare with healthy controls.

PRIMARY OBJECTIVE

To compare the neurocognitive functions of clinically stable Schizophrenia patients with that of healthy age and gender matched controls.

SECONDARY OBJECTIVES

1. To compare the neurocognitive functioning between patients with less than 2 years duration of illness and more than 2 years duration of illness among the Schizophrenia group.

2. To correlate the neurocognitive functions and disability among clinically stable schizophrenia patients.

METHODOLOGY

STUDY DESIGN

It is a Cross-sectional study design. Convenient sampling was done for recruitment of participants. The total number of participants recruited is 40, among which 20 were clinically stable schizophrenia patients and 20 were age and gender matched healthy controls. The study was conducted at PSG hospital, Peelamedu. The study was conducted from July 2017 to August 2018. The assessment

STUDY PARTICIPANTS

The participants were recruited from Out Patient Services in the Department of Psychiatry at PSG Institute of Medical Sciences and Research. The Schizophrenia group consisted of patients visiting the out-patient department during their routine clinical visit.

The healthy control group consisted of participants who were relatives of in-patients in our hospital or hospital staff. The control group was matched for age and gender with the Schizophrenia group.

INCLUSION CRITERIA FOR PATIENTS

- Age of 18 to 60 years
- Patients who qualify for the diagnosis of Schizophrenia according to ICD 10 criteria, currently stable
- Patients without any other psychiatric diagnoses as per MINI
- Patients who can read English/ Tamil
- Remission criteria: PANSS (Positive and Negative Syndrome Scale) score of less than or equal to 3 each, on items 1-3 of positive subscale, on items 1,4 & 6 of negative subscale, on items 5 & 9 of general psychopathology subscale, in the previous 3 months.

EXCLUSION CRITERIA FOR PATIENTS

- Patients with significant comorbid organic conditions
- Substance dependence except nicotine dependence
- Low vision, color blindness
- Patients with significant movement disorder
- Mental retardation

INCLUSION CRITERIA FOR CONTROLS

- Age of 18 to 60 years
- Participants without any psychiatric diagnoses as per MINI
- Participants who can read English/ Tamil
- Participants with normal vision, without color blindness

EXCLUSION CRITERIA FOR CONTROLS

- Participants with significant comorbid organic condition
- Substance dependence except nicotine dependence
- Low vision, color blindness
- Mental retardation

Participants who fulfilled the inclusion & exclusion criteria and gave written informed consent to participate in the study were recruited.

TOOLS TO BE USED

PANSS

The Positive and Negative Syndrome Scale (Stanley Kay, Lewis Opler, and Abraham Fiszbein, 1987) is a scale to measure the symptom severity in Schizophrenia. It has 30 items, out of which 7 constitutes the Positive symptoms scale, 7 constitutes Negative symptoms scale and the remaining 16 constitutes the General Psychopathology scale.

Each item is scored on a scale of 1 to 7, with 1 being absent and 7 being extreme. In our study, this scale was used to assess the remission in schizophrenia patients, according to the Remission Criteria given by Nancy Andreasen et al. (2005). As per the criteria, scores less than or equal to 3 on selected items of the PANSS scale is required for remission. [11]

The items include:

- Delusions (P1), Conceptual disorganization (P2) and Hallucinatory behavior (P3) of the Positive symptom subscale
- Blunted affect (N1), Social withdrawal (N4) and Lack of Spontaneity (N6) of the Negative symptom subscale
- Mannerism / Posturing (G5) and Unusual thought content (G9) of the General Psychopathology subscale

The PANSS rating was done by the researcher on all the schizophrenia patients recruited for the study. Fulfilling the above criteria for the last 3 months before participation in the study is considered as remission / clinically stable schizophrenia.

M.I.N.I.

The Mini International Neuropsychiatric Interview (M.I.N.I. 5.0) is a brief structured interview for the major Axis I psychiatric disorders in DSM-IV and ICD-10. It is a

clinical interview with very precise questions about psychological problems which require a yes or no answer. The M.I.N.I. is divided into modules, each corresponding to a diagnostic category. At the beginning of each diagnostic module screening question(s) corresponding to the main criteria of the disorder are given. At the end of each module, diagnostic box(es) permit the clinician to indicate whether diagnostic criteria are met. All questions must be rated based on the yes/no answer.

Both Schizophrenia patient group and the healthy control group were required to undergo screening with M.I.N.I to rule out any major psychiatric disorders. M.I.N.I. was applied on both schizophrenia patient group and healthy control group by the researcher.

NIMHANS NEUROPSYCHOLOGICAL BATTERY

This Neuropsychological Battery to assess the neurocognitive functions was developed by the National Institute of Mental Health and Neuro Sciences (Rao, Subbakrishna, Gopukumar, 2004). We decided to use this battery, rather than any other Internationally used neuropsychological assessment tool, as those tools developed in western countries cannot be used in our Indian population without slight modifications in the tests; alsothe normative data for scoring may not be valid in an Indian context. Thus, the NIMHANS Neuropsychological Battery was developed with normative data for our population and validated for use internationally, which will be used for our study. The tool has a specificity of about 85%. [12]

The battery has a list of 19 tests to assess seven cognitive domains such as speed, attention, executive functions, comprehension, verbal learning and memory, visuo-spatial construction and visual learning and memory.

For our study, we selected 8 tests that assessed five neurocognitive domains – speed, attention, executive function, verbal learning and memory, visual learning and memory and visuo-spatial construction.

S.No	COGNITIVE DOMAIN	FUNCTION	NAME OF THE TEST
1.	**Speed of Processing**	Mental speed	Digit symbol substitution test
2.	**Attention**	Sustained attention	Digit vigilance test
3.	**Executive functions**	Verbal fluency	Controlled Oral Word Association Test (COWA)
4.		Category fluency	Animal naming test
5.		Working memory	Verbal N back test
6.		Response inhibition	Stroop test
7.	**Learning and memory**	Verbal	Auditory Verbal Learning test
8.	**Visuo-spatial construction** **Visual learning & memory**	Visual	Complex figure test

DIGIT SYMBOL SUBSTITUTION TEST

This assesses visuo-motor coordination, motor persistence, sustained attention and speed of processing. It consists of numbers 1 to 9 in 100 squares arranged randomly in 4 rows in a sheet of paper. Each number is assigned a symbol, which is given at the top of the page. The participant is required write the respective symbols under each digit. The instructions are explained by the researcher and the first ten squares are done as practice with the researcher's help. After that, the participant is asked to do on their own by filling the symbols row-wise and to do as fast as possible. The researcher notes down the time taken to finish the task and the errors made are also noted down.

DIGIT VIGILANCE TEST

This is a test for sustained attention. The test consists of a sheet of randomly arranged digits from 1-9. The sheet has 50 rows and each row has 30 digits which are closely placed to each other. The researcher instructs the participant to mark two target digits (1 & 5) by making a '/' symbol over the digits. The first row can be done for practice with the resesarcher's help. The participant is asked to work row by row, and to do as fast as possible without missing the target digits or mark non-target digits. After the task is completed, the total time taken by the participant is noted. Both omission and commission type of errors are also noted down and counted how many are made in total.

CONTROLLED ORAL WORD ASSOCIATION TEST (COWA)

It is a test of phonemic fluency. It measures one's ability to generate words based on phonetic similarity. The researcher is to instruct the participants to generate as many new words as possible in 60 seconds, that starts with consonants F, A and S. For non-English speaking participants in India, consonants such as 'Ka', 'Pa', 'Ma' are given and asked to generate words in their mother tongue. While using consonants from their mother tongue, the various inflections of the same letter can also be used to generate new words – for example, Ka, Kaa, Ki, Kee, Ku, Ke, etc. Before starting the test, a practice test can be done using another consonant which is not used for the actual test. The participant is instructed not to generate proper nouns such as names of person or place, names of numbers or series of words by changing only the suffix (eg., fast, faster, fastest). The three consonants are given one after another, with a short pause after each completing each consonant. The researcher notes down all the words generated, counts the number of acceptable words for each consonant and then calculate the average number of new words generated over the 3 consonants.

ANIMAL NAMING TEST

This is a test for category fluency, which is a form of verbal fluency. It measures the ability of a person to generate words belonging to a particular semantic category. In this test, the participant is given 60 seconds and asked to generate the names of animals, but not names of fish, birds, insects or snakes. The participant is asked not to repeat the same name twice. The animal names generated are noted down and the total number of new words generated forms the score.

VERBAL N BACK TEST

It is a test of externally guided working memory. It has 2 versions – Verbal 1 back and Verbal 2 back tests.

VERBAL 1 BACK TEST

This test involves verbal storage and rehearsal. It assesses the verbal working memory. The test comprises of a list of 30 randomly selected and arranged consonants which are common to multiple Indian languages. Of these, nine consonants are repeated consecutively in the list. The participant is instructed to tap once when he/she hears the same consonant being repeated consecutively. A practice test is given by the researcher, consisting of 4 consonants with 1 consonant being repeated consecutively. While presenting the list of consonants, the number of correct and incorrect responses are noted down. The number of correct responses is the number of hits. The number of incorrect responses or missing to make a correct response is the number of errors – commission and omission errors.

VERBAL 2 BACK TEST

This test requires verbal storage and rehearsal and manipulation of information. It tests the central executive working memory. Similar to Verbal 1 back test, this test comprises of a different set of 30 randomly selected and arranged consonants common to multiple Indian languages. Of these, nine consonantly are repeated consecutively with an intervening consonant between the consecutive repetition (eg.,

La-Kha-La). The participant is instructed to tap when he/she hears the same consonant consecutively with an intervening consonant. A practice test is given by the researcher with list 4 consonants, wherein 1 consonant is repeated consecutively. The test list of consonants is then presented and the number of correct responses, omission and commission errors are noted down. The number of correct responses is the total number of hits.

STROOP TEST

This is a test for response inhibition, which is an executive function. It consists of a sheet of paper with a list of randomly arranged words such as “RED”, “GREEN”, “BLUE” and “YELLOW” printed in colored text and in capital letters. The color of the text occasionally corresponds to the word printed. First, the participant is instructed to read the words in the list column-wise. Then, the participant is instructed to name the color of the text from the same list and he/she can repeat the response in case of a wrong response. A practice test can be given for first 5 words. The time taken for both tasks is noted down. The time taken to name the color of the text will be more than the time taken to read the words. The difference between the two is the “Stroop effect”. The Stroop effect in seconds is calculated.

AUDITORY VERBAL LEARNING TEST

This is a test for verbal learning and memory. It assesses the capacity to learn and remember verbal material. This test is an adaptation of Rey's Auditory Verbal Learning Test (AVLT) and is available in translated versions in 4 Indian languages – Hindi, Tamil, Telugu and Kannada. The test consists of two separate lists of 15 words each and these words can be names of familiar objects like vehicles, body parts, tools and animals. At first, list A consisting of 15 words is presented to the participant and after completion of the list, he/she is asked to recall as many words as possible. Similarly, five consecutive trials are given and the number of words recalled is noted down for each trial. After the five trials, list B consisting of a different set of 15 words is presented to the participant and he/she is asked to recall words from list B immediately. After this interference, immediate recall of list A is done. Twenty minutes later, during which time, others non-verbal tasks can be done, the delayed recall of list A is assessed. After the delayed recall, a list of 30 words, out of which 15 are from list A is presented to the participant. Whenever a word from list A is presented, the participant is asked to tap on the table. This tests the recognition. The total number of correct hits, omission and commission errors are noted down.

Learning score comprises the number of words recalled correctly in each of the first five trials and the total number of words recalled over the five trials. Memory score comprises the number of words recalled correctly in the immediate recall of list A and B, delayed recall of list A and recognition trial. Long Term Percent Retention (LTPR) is the percentage score calculated by the formula –

(Delayed recall score/Trial 5 score) X 100

COMPLEX FIGURE TEST (Rey's)

This is a test for visuo-constructive ability and visual learning and memory. The test consists of three trials – the copying trial, the immediate recall trial and the delayed recall trial. It is done using a complex, abstract design with multiple subcomponents, which is presented to the participant only once during the copying trial. First, the participant is asked to copy this complex figure on a piece of paper free-hand. An eraser can be used. This tests the visuo-constructive ability. After a three minutes interval during which time, other simple tasks from the battery can be done, the immediate recall is assessed by asking the participant to reproduce the figure as accurately as possible. Then, following 30 minutes interval, during which time other verbal tasks are to be done, delayed recall is assessed by asking the participant to reproduce the figure as accurately as possible.

Each of the three trials is scored depending upon the accuracy of the figure and placement of the component parts of the figure.

SCORING OF NEUROPSYCHOLOGICAL TESTS

After the completion of all tasks, the individual scores and the number of errors from each test is noted down. These scores are matched against the normative data table given in the battery. The percentile scores are then obtained based on the age, gender and educational status of the participant.

In our study, the researcher took training on how to perform the neuropsychological tests needed for our study, from a Clinical Psychologist who holds a Ph.D. in Clinical Psychology. Under the supervision of the Clinical Psychologist, neuropsychological assessment was done by the researcher for five normal volunteers, before the initiation of the study. For the study, the neuropsychological assessment and scoring was done by the researcher.

IDEAS

The Indian Disability Evaluation and Assessement Scale (IDEAS) was developed by the Rehabilitation Committee of the Indian Psychiatric Society in the year 2000. It is a scale for assessing and quantifying disability in patients with mental illnesses. This scale is validated and best suited for using in the Indian population.

The scale consists of 4 domains – Self-care, Interpersonal activities, Communication & Understanding and Work. The scale also gives a list of guiding questions for assessing disability in each domain. Each domain is scored on a scale of 0 to 4 wherein, 0 means no disability and 4 means profound disability. The sum of the scores on all the 4 domains constitutes the total score.

Depending on the duration of illness, an additional score of 1 to 4 has to be added, where 4 is for duration of illness more than 10 years. This is the 'Duration of illness' score.

The global disability score is the sum of Total score and Duration of illness score. This can range from 0 to 20. A score of 0 means No disability and 20 means profound disability. Higher the score, more is the disability.

A global disability percentage is also given based on this Global disability score.

Global score	**:**	**Global Disability Percentage Score**
0	:	0% = No disability
1 to 6	:	< 40 % = Mild disability
7 to 13	:	40 to 70 % = Moderate disability
14 to 19	:	71 to 99 % = Severe disability
20	:	100% = Profound disability

According to this scale, a global disability percentage of 40% and above is the cut-off to be eligible for welfare measures given by the Government of India.

All the participants in the Schizophrenia group were scored on the IDEAS and Global Disability Percentage score was calculated. The scoring was done by the Primary Investigator based on the interview, reports from the care-giver and medical records from the patient's hospital file.

The tools were applied for the schizophrenia group and control group as follows:

SCHIZOPHRENIA GROUP	CONTROL GROUP
PANSS	M.I.N.I.
↓	↓
M.I.N.I.	↓
↓	↓
NIMHANS Neuropsychological Battery	NIMHANS Neuropsychological Battery
↓	
IDEAS	

Ethical approval was obtained for the study from the Institutional Human Ethics Committee of PSG Institute of Medical Sciences and Research.

SAMPLE SIZE ESTIMATION

Considering the similar previous studies and number of patients attending our OPD from previous statistics, we decided to have a sample of twenty schizophrenia patients and twenty age and gender matched healthy controls.

STATISTICAL ANALYSIS

All calculations were performed using IBM SPSS Statistics (version 20.0 SPSS Inc., Chicago, IL, USA).

In the test of normality as assessed by Shapiro-Wilk test, the normalityof distribution of variables under interest is tested, by comparing the correlation of the data (variables of interest) with the corresponding normal scores. The pvalues of most of the variables are >0.05, which indicates that thesevariables are normally distributed across the cases & controls and thusparametric test were used for analysis.

Outlier is the extreme value which does not correlate with other value in the variable. Box-and-whisker plots graph depicted that the majority of the scores of neuropsychological tests have no outlier observation/negligible amount of outlier observation. Hence, further analysis was carried out.

In both groups (schizophrenia patients and healthy controls), socio demographic variables, neuropsychological test scores, functioning scores were assessedusing relative and absolute frequencies, means, and standard deviations, whichever deemed appropriate.

Comparison between the schizophrenia group and control group, and within the schizophrenia group (<2 years Vs >2 years duration of illness) regarding

neuropsychological test scores and sub-group analyses based on age, gender and educational status were done using Independent sample t test (for discrete variables) and ANOVA (Analysis of Variance) test (for continuous variables). The level of statistical significance was set at 5% i.e., $p<0.05$.

For analysis of correlation between the disability assessment scores and neuropsychological test scores, Pearson correlation analysis was used with statistical significance set at $p<0.05$.

RESULTS

SECTION I: SOCIODEMOGRAPHIC VARIABLES

TABLE 1.1: DEMOGRAPHIC DETAILS OF SCHIZOPHRENIA PATIENT GROUP AND HEALTHY CONTROL GROUP

Socio-Demographic details	Schizophrenia group	Control group
Gender		
Male	9 (45)	9 (45)
Female	11 (55)	11 (55)
Total	20 (100)	20 (100)
Age group		
18-30	8 (40)	8 (40)
31-50	10 (50)	10 (50)
51-65	2 (10)	2 (10)
Total	20 (100)	20 (100)
Education level		
School level	12 (60)	9 (45)
College level	8 (40)	11 (55)
Total	20 (100)	20 (100)
Marital status		
Married	10 (50)	14 (70)
Unmarried	8 (40)	6 (30)
Separated	2 (10)	-
Total	20 (100)	20 (100)
Occupation Status		
Working	7 (35)	15 (75)

Not working	13 (65)	5 (25)
Total	20 (100)	20 (100)
Duration of illness		
Patients with duration of illness <2 years	8 (40)	-
Patients with duration of illness >2 years	12 (60)	-
Total	20 (100)	-

Table 1 presents the demographic details of the 2 groups - schizophrenia patients group and healthy controls group. The total number of participants of the study are 40. Among the 40 participants, 20 are clinically stable schizophrenia patients and 20 age and gender matched healthy controls.

The mean age of the participants is 35.5 years, half of the total number of participants aged 31-50 years, followed by 40% aged between 18-30 years and only 10% aged between 51-65 years.

There were almost equal number of male and female participants, with females being 55% and males being 45%.

In schizophrenia group, 50% of the participants were married and 50% were unmarried or separated. In the control group, 70% of participants were married.

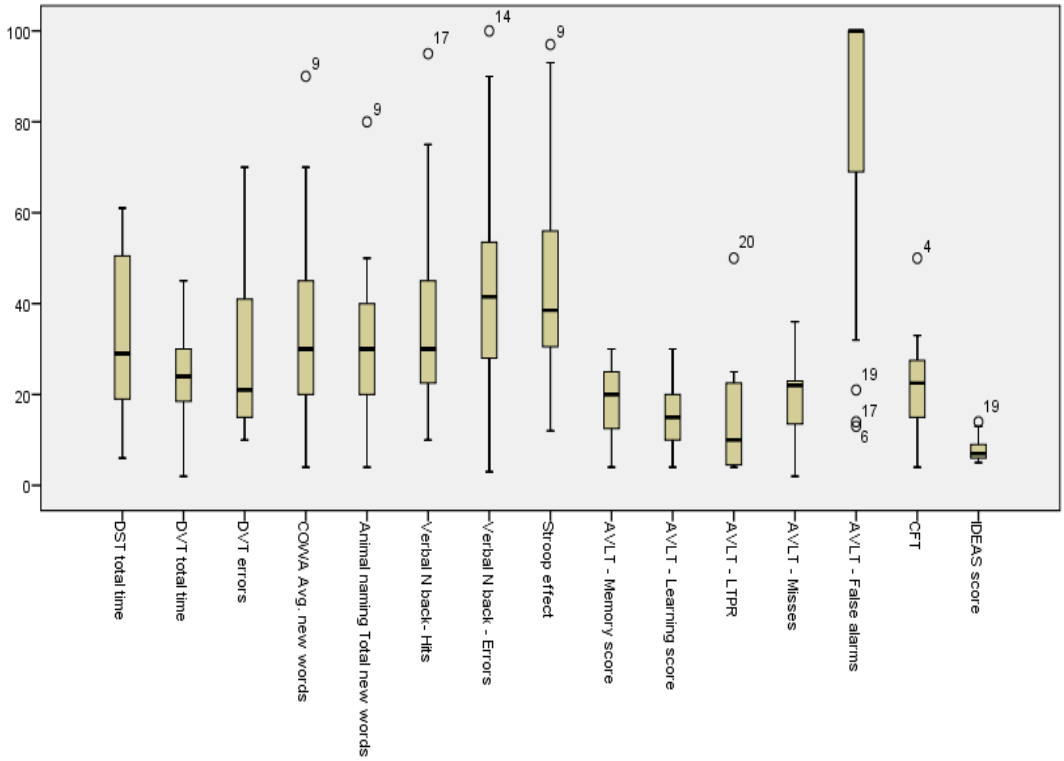
The majority of participants in the schizophrenia group (60%) completed school level education while the majority in the control group has completed college level education (55%).

Among the schizophrenia patients, 60% have duration of illness more than 2 years with mean duration of as 10.3 years, whereas 40% have duration of illness less than 2 years with mean duration of 14.25 months.

In the schizophrenia patients group, the mean duration of untreated psychosis i.e., before initiation of treatment is 19.7 months.

SECTION II: OUTLIER IDENTIFICATION IN THE DATA OF NEUROPSYCHOLOGICAL TEST SCORES

FIGURE I: BOX-AND-WHISKER PLOT GRAPH FOR OUTLIER IDENTIFICATION



The above figure depicts that the majority of data of the neuropsychological test scores have no outlier observation/negligible amount of outlier observation.

SECTION III: COMPARISON OF SCHIZOPHRENIA PATIENTS AND HEALTHY CONTROL GROUP

TABLE 3.1 - DIFFERENCE IN THE SCORES OF NEUROPSYCHOLOGICAL TESTS BETWEEN SCHIZOPHRENIA PATIENT GROUP AND HEALTHY CONTROL GROUP

Neuropsychological tests	**Schizophrenia**	**Controls**	**t-Value**	**P-value**
	Mean±Sd			
DST total time	32.65±17.62	66.95±7.61	-7.992	0.001**
DVT total time	24.20±10.49	57.75±9.54	-10.580	0.001**
DVT errors	28.45±18.52	22.90±9.88	1.183	0.247
COWA Avg. new words	34.20±20.23	64.00±13.92	-5.428	0.001**
Animal naming Total new words	31.45±16.87	61.75±14.89	-6.021	0.001**
Verbal N back- Hits	36.50±20.72	54.75±13.90	-3.271	0.002**
Verbal N back - Errors	45.05±24.94	59.35±27.28	-1.730	0.092
Stroop effect	45.05±23.80	73.95±7.07	-5.206	0.001**
AVLT - Memory score	18.90±8.85	62.00±17.04	-10.036	0.001**
AVLT - Learning score	14.90±7.40	57.00±16.09	-10.629	0.001**
AVLT - LTPR	14.50±11.64	55.25±16.02	-9.204	0.001**
AVLT - Misses	20.05±10.16	34.55±24.41	-2.452	0.021*
AVLT - False alarms	80.90±34.32	88.85±23.01	-0.860	0.396
CFT	21.30±10.94	55.50±14.95	-8.258	0.001**

****P<0.01; *P<0.05**

Table 8.2 shows that, on comparing the neuropsychological test scores between the schizophrenia group and healthy control group, the schizophrenia group obtained

statistically significant ($p<0.05$) poorer scores than the control group in Digit Substitution test (DST) total time, Digit Vigilance Test (DVT) total time, Controlled Oral Word Association (COWA) test- Average New Words, Animal naming test – Total New Words, Verbal N back Hits, Stroop effect, Auditory Verbal Learning Test (AVLT) Memory score, AVLT Learning score, AVLT Long Term Percent Retention (AVLT-LTPR), AVLT Misses and Complex Figure Test (CFT). The means and standard deviations of the scores obtained by the two groups are given in the table above.

There was no statistically significant difference between the scores of the two groups in Digit Vigilance Test errors, Verbal N Back Errors and Auditory Verbal Learning Test False alarms ($p>0.05$)

FIGURE 2 : MEAN SCORES CHART FOR THE NEUROPSYCHOLOGICAL TESTS' SCORES IN SCHIZOPHRENIA PATIENTS GROUP AND HEALTHY CONTROL GROUP

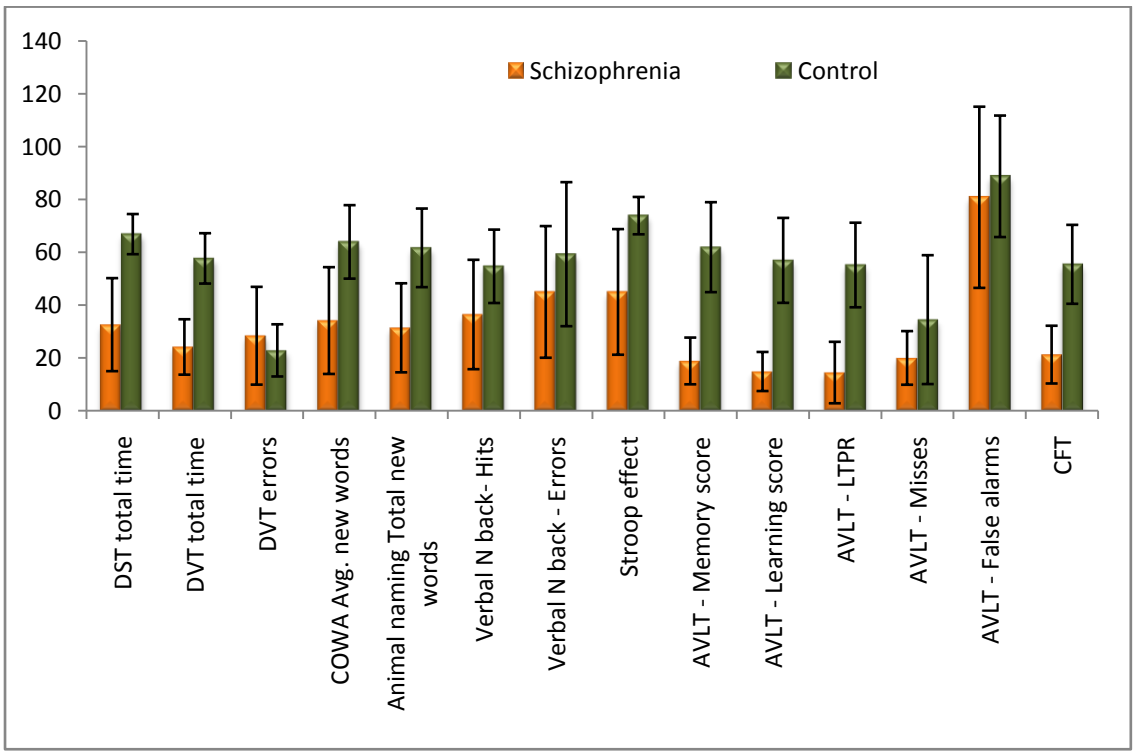


TABLE 3.2: DIFFERENCE IN THE SCORES OF NEUROPSYCHOLOGICAL TESTS BETWEEN MALE SCHIZOPHRENIA GROUP AND MALE CONTROL GROUP

Neuropsychological tests	**Male Schizophrenia group**	**Male Control**	**t-Value**	**P-value**
	Mean±Sd			
DST total time	33.78±21.17	69.11±7.67	-4.707	0.001**
DVT total time	24.33±13.69	53.00±7.65	-5.483	0.001**
DVT errors	29.89±21.91	24.89±10.41	0.618	0.545
COWA Avg. new words	32.78±11.49	68.33±13.46	-6.027	0.001**
Animal naming Total new words	36.11±7.82	64.44±17.58	-4.418	0.001**
Verbal N back- Hits	37.78±24.51	55.00±16.58	-1.746	0.100
Verbal N back - Errors	39.67±17.81	54.78±27.73	-1.375	0.188
Stroop effect	38.00±9.07	75.22±5.45	-10.554	0.001**
AVLT - Memory score	21.56±8.55	65.56±16.09	-7.244	0.001**
AVLT - Learning score	17.78±5.07	57.22±16.97	-6.679	0.001**
AVLT - LTPR	14.33±8.96	53.33±18.71	-5.641	0.001**
AVLT - Misses	24.89±6.95	32.56±25.73	-0.863	0.401
AVLT - False alarms	73.22±40.52	87.44±24.94	-0.897	0.383
CFT	20.33±14.94	58.33±16.22	-5.172	0.001**

**P<0.01; *P<0.05

From the above table, it is inferred that there is a statistically significant difference between male schizophrenia patients group and male control group in the scores of DST total time, DVT total time, COWA average new words, animal naming total new words, stroop effect, AVLT-memory score, AVLT-learning score, AVLT-LTPR and CFT scores and this difference is also statistically significant ($p<0.05$). In addition, the mean scores of the tests reveal that male control group people have high scores in the majority of the verbal and non-verbal tasks (except Verbal N Back Hits) i.e. male schizophrenia patients group have poorer cognitive performance when compared with male control group. The mean scores and standard deviations of each test is given in the table.

TABLE 3.3: DIFFERENCE IN THE SCORES OF NEUROPSYCHOLOGICAL TESTS BETWEEN FEMALE SCHIZOPHRENIA GROUP AND FEMALE CONTROL GROUP

Neuropsychological tests	**Female Schizophrenia group**	**Female Control**	**t-Value**	**P-value**
	Mean±Sd			
DST total time	31.73±15.14	65.18±7.44	-6.577	0.001**
DVT total time	24.09±7.70	61.64±9.44	-10.224	0.001**
DVT errors	27.27±16.25	21.27±9.61	1.054	0.305
COWA Avg. new words	35.36±25.85	60.45±13.86	-2.836	0.010**
Animal naming Total new words	27.64±21.36	59.55±12.74	-4.255	0.001**
Verbal N back- Hits	35.45±18.23	54.55±12.14	-2.891	0.009**
Verbal N back - Errors	49.45±29.68	63.09±27.66	-1.115	0.278
Stroop effect	50.82±30.48	72.91±8.28	-2.320	0.040*
AVLT - Memory score	16.73±8.88	59.09±18.00	-7.000	0.001**
AVLT - Learning score	12.55±8.37	56.82±16.17	-8.066	0.001**
AVLT - LTPR	14.64±13.90	56.82±14.19	-7.043	0.001**
AVLT - Misses	16.09±10.92	36.18±24.41	-2.492	0.022*
AVLT - False alarms	87.18±28.77	90.00±22.47	-0.256	0.801
CFT	22.09±6.86	59.18±14.19	-6.542	0.001**

**P<0.01, *P<0.05

Similar to the results from comparison of schizophrenia group and control group, on comparison of female schizophrenia patients group and female control group, the female schizophrenia group scored lower on DST total time, DVT total time, COWA

average new words, animal naming total new words, verbal N back-hits, stroop effect, AVLT-memory score, AVLT-learning score, AVLT-LTPR and CFT scores. This difference in scores was found to be statistically significant ($p<0.05$). The mean scores and standard deviations of each test is given in the table. reveal that female schizophrenia patients group have low level of cognitive compared with female control group.

TABLE 3.4: DIFFERENCE IN THE SCORES OF NEUROPSYCHOLOGICAL TESTS BETWEEN SCHOOL-LEVEL EDUCATED SCHIZOPHRENIA GROUP AND CONTROL GROUP

Neuropsychological tests	**School-level educated Schizophrenia group**	**School-level educated Control**	**t-Value**	**P-value**
	Mean±Sd			
DST total time	26.08±10.99	62.88±6.11	-9.012	0.001**
DVT total time	25.67±6.00	58.33±10.56	-8.326	0.001**
DVT errors	24.58±13.28	26.33±8.47	-0.345	0.734
COWA Avg. new words	30.33±18.40	63.89±13.64	-4.594	0.001**
Animal naming Total new words	23.25±12.07	54.44±13.33	-5.605	0.001**
Verbal N back- Hits	36.67±25.88	47.78±13.94	-1.163	0.259
Verbal N back - Errors	48.08±28.82	68.67±27.49	-1.651	0.115
Stroop effect	43.50±26.09	71.89±7.78	-3.563	0.005**
AVLT - Memory score	16.50±9.84	61.11±19.49	-6.292	0.001**
AVLT - Learning score	12.75±8.56	58.33±16.20	-7.675	0.001**
AVLT - LTPR	15.58±13.17	57.22±15.63	-6.621	0.001**
AVLT - Misses	18.67±11.91	30.67±13.28	-2.176	0.042*
AVLT - False alarms	75.33±36.89	88.11±23.75	-0.963	0.348
CFT	19.50±8.54	55.56±15.09	-6.956	0.001**

**P<0.01; *P<0.05

From the above table, it is inferred that there is a statistically significant difference ($p<0.05$) between the scores of school-level educated schizophrenia patients group and school- level educated control group on the following scores: of DST total time, DVT total time, COWA average new words, animal naming total new words, stroop effect, AVLT-memory score, AVLT-learning score, AVLT-LTPR, AVLT-Misses and CFT scores. It is found that the school-level educated schizophrenia group showed a poorer performance than the school-level educated control group. There was no statistically significant difference in the performance on Verbal N back test Hits. The mean scores and standard deviations of each test is given in the table.

TABLE 3.5: DIFFERENCE IN THE SCORES OF NEUROPSYCHOLOGICAL TESTS BETWEEN COLLEGE LEVEL EDUCATED SCHIZOPHRENIA GROUP AND CONTROL GROUP

Neuropsychological tests	**College-level educated Schizophrenia group**	**College-level educated Control**	**t-Value**	**P-value**
	Mean±Sd			
DST total time	42.50±21.63	70.27±7.29	-3.491	0.008**
DVT total time	22.00±15.27	57.27±9.11	-6.308	0.001**
DVT errors	34.25±24.28	20.09±10.43	1.549	0.156
COWA Avg. new words	40.00±22.68	64.09±14.80	-2.809	0.012**
Animal naming Total new words	43.75±15.98	67.72±13.85	-3.495	0.003**
Verbal N back- Hits	36.25±10.61	60.45±11.50	-4.675	0.001**
Verbal N back - Errors	40.50±18.55	51.73±25.84	-1.045	0.311
Stroop effect	47.37±21.39	75.63±6.28	-4.182	0.001**
AVLT - Memory score	22.50±5.98	62.73±15.71	-7.756	0.001**
AVLT - Learning score	18.12±3.72	55.91±16.71	-7.258	0.001**
AVLT - LTPR	12.87±9.49	53.63±16.89	-6.126	0.001**
AVLT - Misses	22.12±7.02	37.73±31.08	-1.609	0.135
AVLT - False alarms	89.25±30.41	89.45±23.53	-0.017	0.987
CFT	24.00±14.00	55.45±15.56	-4.531	0.001**

**P<0.01, *P<0.05

Comparison of college-level educated schizophrenia patients and college-level educated control group revealed that college-level educated schizophrenia group had a statistically significant ($p<0.05$) poorer scores on DST total time, DVT total time, COWA average new words, animal naming total new words, verbal N back-hits, stroop effect, AVLT-memory score, AVLT-learning score, AVLT-LTPR and CFT scores. The mean scores and standard deviations of each test is given in the table.

SECTION IV: COMPARING SCHIZOPHRENIA PATIENTS WITH DURATION OF ILLNESS LESS THAN 2 YEARS AND THE PATIENTS WITH DURATION OF ILLNESS MORE THAN 2 YEARS

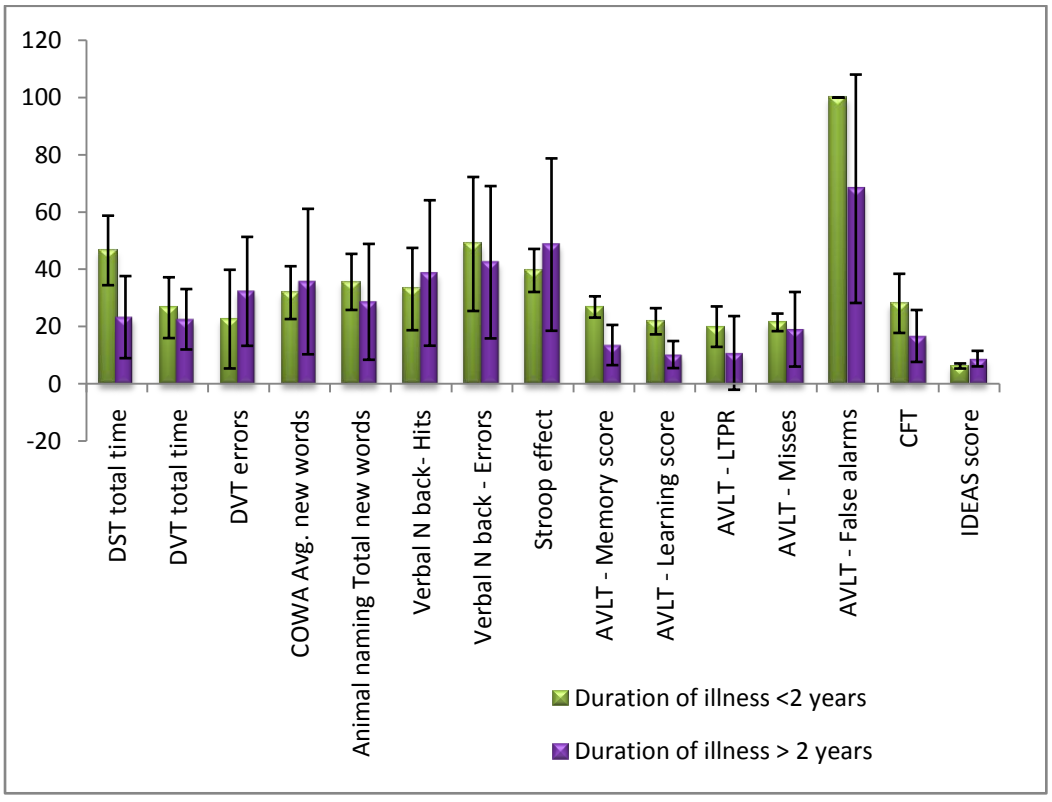
TABLE 4.1: DIFFERENCE IN THE SCORES OF NEUROPSYCHOLOGICAL TESTS BETWEEN SCHIZOPHRENIA PATIENTS WITH DURATION OF ILLNESS BELOW 2 YEARS AND THE PATIENTS WITH DURATION OF ILLNESS ABOVE 2 YEARS

Neuropsychological tests	**Duration of illness <2 years**	**Duration of illness > 2 years**	**t-Value**	**P-value**
	Mean±Sd			
DST total time	46.63±12.15	23.33±14.34	3.772	0.001**
DVT total time	26.63±10.62	22.58±10.55	0.837	0.414
DVT errors	22.63±17.24	32.33±19.03	-1.159	0.262
COWA Avg. new words	31.88±9.23	35.75±25.41	-0.410	0.686
Animal naming Total new words	35.63±9.79	28.67±20.24	0.899	0.381
Verbal N back- Hits	33.13±14.38	38.75±25.41	-0.584	0.566
Verbal N back - Errors	48.88±23.41	42.50±26.61	0.550	0.589
Stroop effect	39.63±7.52	48.67±30.11	-0.825	0.420
AVLT - Memory score	26.88±3.72	13.58±7.02	4.884	0.001**
AVLT - Learning score	21.88±4.58	10.25±4.73	5.450	0.001**
AVLT - LTPR	20.00±7.07	10.83±12.86	1.828	0.084
AVLT - Misses	21.50±3.07	19.08±13.03	0.617	0.548
AVLT - False alarms	100.00±00	68.17±39.90	2.764	0.018*
CFT	28.13±10.33	16.75±9.07	2.602	0.018*
IDEAS score	6.25±0.89	8.83±2.72	-3.051	0.009**

****P<0.01; *P<0.05**

From the above table, it is concluded that there is a statistically significant difference (p<0.05) between the scores of Neuropsychological testsamong schizophrenia patients with duration of illness less than 2 years and the patients with duration of illness more than 2 years, wherein those with >2years duration of illness scored poorer. This difference was seen in the scores of the following: moderately significant - AVLT-false alarms and CFT; highly significant - DST total time, AVLT memory score, AVLT learning score and IDEAS score (P<0.01). However, there is no statistical difference in the scores of DVT total time, DVT errors, COWA average new words, Animal naming total new words, verbal N back hits & errors, stroop effect, AVLT-LTPR and AVLT Misses.

FIGURE 3: MEAN SCORES CHART FOR NEUROPSYCHOLOGICAL TESTS' SCORES IN SCHIZOPHRENIA PATIENTS WITH DURATION OF ILLNESS LESS THAN 2 YEARS AND SCHIZOPHRENIA PATIENTS WITH DURATION OF ILLNESS MORE THAN 2 YEARS



SECTION V: COMPARING THE SCORES OF NEUROPSYCHOLOGICAL TESTS AMONG MALE AND FEMALE SCHIZOPHRENIA PATIENTS

TABLE 5.1: DIFFERENCE IN THE SCORES OF NEUROPSYCHOLOGICAL TESTS BETWEEN SCHIZOPHRENIA MALE AND FEMALE PATIENTS

Neuropsychological tests	Male	Female	t-Value	P-value
	Mean±Sd			
DST total time	33.78±21.17	31.73±15.14	0.252	0.804
DVT total time	24.33±13.69	24.09±7.7	0.050	0.961
DVT errors	29.89±21.91	27.27±16.25	0.307	0.763
COWA Avg. new words	32.78±11.49	35.36±25.85	-0.277	0.785
Animal naming Total new words	36.11±7.81	27.64±21.36	1.220	0.244
Verbal N back- Hits	37.78±24.51	35.45±18.23	0.243	0.811
Verbal N back - Errors	39.67±17.81	49.45±29.68	-0.867	0.397
Stroop effect	38.00±9.07	50.82±30.48	1.325	0.210
AVLT - Memory score	21.56±8.55	16.73±8.88	1.230	0.234
AVLT - Learning score	17.78±5.07	12.55±8.37	1.641	0.118
AVLT - LTPR	14.33±8.96	14.64±13.90	-0.056	0.956
AVLT - Misses	24.89±6.95	16.09±10.92	2.089	0.051
AVLT - False alarms	73.22±40.52	87.18±28.77	-0.900	0.380
CFT	20.33±14.94	22.09±6.86	-0.326	0.751
IDEAS score	6.89±1.83	8.55±2.81	-0.085	0.145

Independent sample t test clearly reveals that there is no statistically significant difference between male and female schizophrenia patients on the scores of all Neuropsychological tests and IDEAS score. ($p>0.05$)

SECTION VI: COMPARING THE SCORES OF NEUROPSYCHOLOGICAL TESTS AMONG SCHOOL-LEVEL EDUCATED SCHIZOPHRENIA PATIENTS AND COLLEGE-LEVEL EDUCATED SCHIZOPHRENIA PATIENTS

TABLE 6.1: DIFFERENCE IN THE SCORES OF NEUROPSYCHOLOGICAL TESTS AMONG SCHOOL LEVEL EDUCATED SCHIZOPHRENIA PATIENTS AND COLLEGE LEVEL EDUCATED SCHIZOPHRENIA PATIENTS

Neuropsychological tests	**School level**	**College level**	**t-Value**	**P-value**
	Mean±Sd			
DST total time	26.08±11.00	42.50±21.63	-1.983	0.077
DVT total time	25.67±6.00	22.00±15.27	0.647	0.535
DVT errors	24.58±13.28	34.25±24.28	-1.028	0.328
COWA Avg. new words	30.33±18.40	40.00±22.68	-1.050	0.308
Animal naming Total new words	23.25±12.08	43.75±15.98	3.272	0.004**
Verbal N back- Hits	36.67±25.88	36.25±10.61	0.043	0.966
Verbal N back - Errors	48.08±28.82	40.50±18.55	0.656	0.520
Stroop effect	43.50±26.09	47.38±21.39	-0.348	0.732
AVLT - Memory score	16.50±9.84	22.50±5.97	-1.538	0.141
AVLT - Learning score	12.75±8.56	18.13±3.72	-1.920	0.073
AVLT - LTPR	15.58±13.17	12.88±9.49	0.500	0.623
AVLT - Misses	18.67±11.91	22.13±7.02	-0.736	0.471
AVLT - False alarms	75.33±36.89	89.25±30.41	-0.883	0.389
CFT	19.50±8.54	24.00±14.00	-0.897	0.382
IDEAS score	8.67±2.84	6.50±1.07	2.401	0.030*

**P<0.01; P<0.05

Independent sample t test is used to analyze and compare the scores between school-level educated schizophrenia patients and college-level educated schizophrenia patients. There is a statistically significant difference in the performance between the two groups on Animal naming test – Total new words and IDEAS score($p<0.05$). In Animal naming test, college-educated schizophrenia patients has higher scores. In IDEAS, school-educated schizophrenia patients have scored higher. However, there is no significant difference in the scores of the rest of the neuropsychological tests between these two groups.

SECTION VII: COMPARING THE SCORES OF NEUROPSYCHOLOGICAL TESTS AMONG DIFFERENT AGE GROUP IN SCHIZOPHRENIA PATIENTS

TABLE 7.1: DIFFERENCE IN THE SCORES OF NEUROPSYCHOLOGICAL TESTS AMONG DIFFERENT AGE GROUP IN SCHIZOPHRENIA PATIENTS

Neuropsychological tests	**18-30 years**	**31-50 years**	**51-65 years**	**P-value**
	Mean±Sd			
DST total time	41.38±18.75	26.40±15.92	29.00±11.31	0.197
DVT total time	24.13±13.76	24.10±9.12	25.00±4.24	0.994
DVT errors	24.88±17.12	33.70±20.31	16.50±9.19	0.401
COWA Avg. new words	34.38±8.21	39.50±24.77	7.00±4.24	0.113
Animal naming Total new words	35.63±9.79	30.40±21.92	20.00±0.0	0.509
Verbal N back- Hits	31.88±14.12	41.50±25.93	30.00±14.14	0.580
Verbal N back - Errors	41.38±21.94	46.30±30.10	53.50±4.95	0.824
Stroop effect	38.38±6.50	49.70±28.29	48.50±51.61	0.616
AVLT - Memory score	26.25±5.17	13.30±6.98	17.50±10.61	0.003**
AVLT - Learning score	21.88±4.58	10.30±4.67	10.00±7.07	0.001**
AVLT - LTPR	19.88±7.38	7.70±3.80	27.00±32.53	0.015*
AVLT - Misses	21.50±3.07	18.10±13.01	24.00±16.97	0.683
AVLT - False alarms	89.25±30.41	78.30±35.48	60.50±55.86	0.564
CFT	25.50±13.44	17.70±8.95	22.50±3.53	0.336
IDEAS score	6.38±1.06	8.40±2.41	10.50±4.95	0.055*

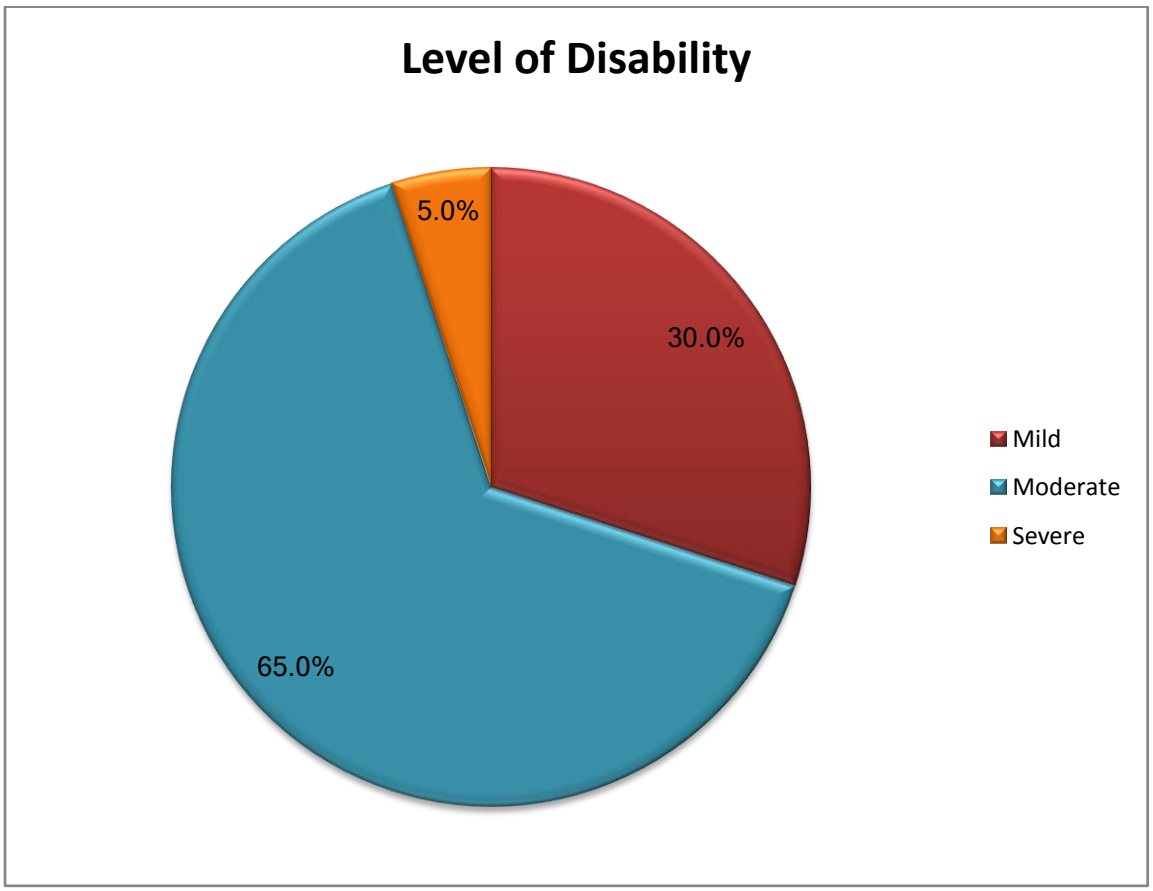
**P<0.01; *P<0.05

Analysis of variance (ANOVA) test has been used to determine the difference in the scores of the neuropsychological tasks among different age groups of schizophrenia

patients. The statistically significant difference was seen among the different age groups in AVLT memory score, AVLT learning score and AVLT LTPR. The schizophrenia patients in the age group 18-30 years have the highest scores in AVLT memory score and AVLT learning score. The mean and standard deviations of the scores are given in the above table.It was also seen that, schizophrenia patients in 18-30 years group have milder disability, patients in 31-50 years have moderate level of disability and patients in 51-65 years group have severe disability.

SECTION VIII: RELATIONSHIP BETWEEN DISABILITY SCORES AND NEUROCOGNITIVE TEST SCORES AMONG SCHIZOPHRENIA PATIENTS

FIGURE 4: PIE CHART FOR PERCENTAGE OF DISABILITY IN SCHIZOPHRENIA PATIENTS



It is noted from the above figure that 65% of schizophrenia patients have a disability score percentage > 40%, thus making this 65% eligible for the welfare measures given by the Government of India.

TABLE 8.1: CORRELATION BETWEEN SCORES IN EACH DOMAIN OF IDEAS AND NEUROCOGNITIVE TESTS' SCORES IN THE SCHIZOPHRENIA PATIENTS

Neuropsychological tests	IDEAS self-care	IDEAS interpersonal activities	IDEAS communication & interaction	IDEAS work
	r-value (P-value)			
DST total time	-.021 (0.930)	-.078 (0.743)	-.189 (0.425)	-.484 (0.031*)
DVT total time	-.128 (0.590)	.259 (0.270)	-.042 (0.861)	-.356 (0.123)
DVT errors	-.035 (0.883)	-.302 (0.196)	-.584 (0.007**)	.307 (0.188)
COWA Avg. new words	-.021 (0.931)	-.318 (0.172)	-.134 (0.573)	-.220 (0.352)
Animal naming Total new words	-.204 (0.389)	-.238 (0.312)	-.278 (0.235)	-.073 (0.760)
Verbal N back- Hits	-.217 (0.359)	-.010 (0.967)	.305 (0.191)	-.226 (0.339)
Verbal N back - Errors	.162 (0.494)	-.287 (0.220)	.058 (0.809)	-.435 (0.055)
Stroop effect	-.138 (0.561)	-.373 (0.105)	-.338 (0.144)	-.262 (0.264)
AVLT - Memory score	-.339 (0.144)	-.200 (0.397)	-.387 (0.091)	-.222 (0.346)
AVLT - Learning score	-.384 (0.094)	-.172 (0.467)	-.368 (0.111)	-.002 (0.994)
AVLT - LTPR	-.399 (0.082)	-.188 (0.428)	-.179 (0.451)	-.270 (0.250)
AVLT - Misses	-.126 (0.596)	.059 (0.806)	.342 (0.140)	.272 (0.246)
AVLT - False alarms	.021 (0.931)	-.049 (0.837)	-.333 (0.151)	-.365 (0.114)
CFT	-.054 (0.822)	-.041 (0.862)	-.207 (0.380)	-.213 (0.367)

**P<0.01, *P<0.05

Pearson correlation coefficient values indicate that IDEAS score in each domain such as self-care and interpersonal activities does not have a linear relationship with any of the neuropsychological test scores. However, the disability score in the domain 'Communication and Understanding' is seen to have a linear negative relationship with DVT errors and the disability score in the domain 'Work' has a linear negative relationship with DST total time.

TABLE 8.2: CORRELATION BETWEEN IDEAS GLOBAL SCORE AND NEUROPSYCHOLOGICAL TESTS' SCORES IN THE SCHIZOPHRENIA PATIENTS

Neuropsychological tests	**IDEAS Global score**	
	r-value	**P-value**
DST total time	-.537	.015*
DVT total time	-.191	.421
DVT errors	-.092	.699
COWA Avg. new words	-.231	.327
Animal naming Total new words	-.292	.212
Verbal N back- Hits	.037	.879
Verbal N back - Errors	-.201	.395
Stroop effect	-.251	.287
AVLT - Memory score	-.635	.003**
AVLT - Learning score	-.591	.006**
AVLT - LTPR	-.406	.076
AVLT - Misses	.203	.391
AVLT - False alarms	-.489	.028*
CFT	-.453	.045*

**P<0.01; *P<0.05

The statistical significance (P<0.05) clearly reveals there is a linear relationship between the disability score (IDEAS global score) and the scores of

neuropsychological tests such as DST total time, AVLT-memory score, AVLT-learning score, AVLT-False alarms and CFT. Pearson correlation coefficient values of these variables are negative that implies such relationship is negative. i.e., The disability score decreases when the neuropsychological tests' (mentioned above) score increases.

Figure 5: Relationship between DST total time and IDEAS Global score

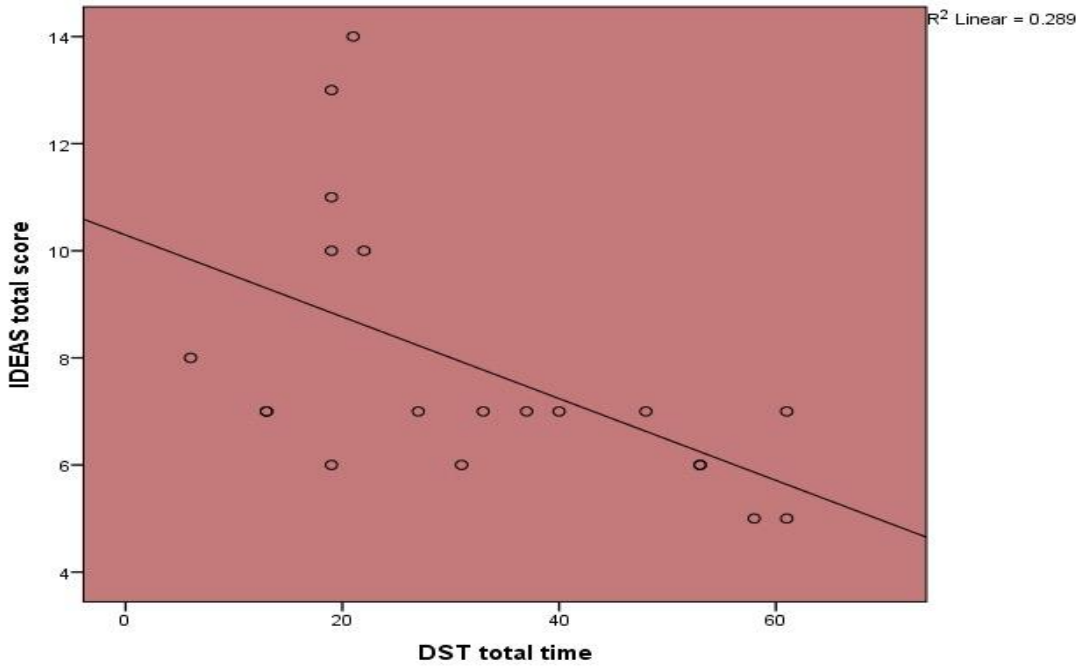


Figure 6: Relationship between AVLT-memory score and IDEAS Global score

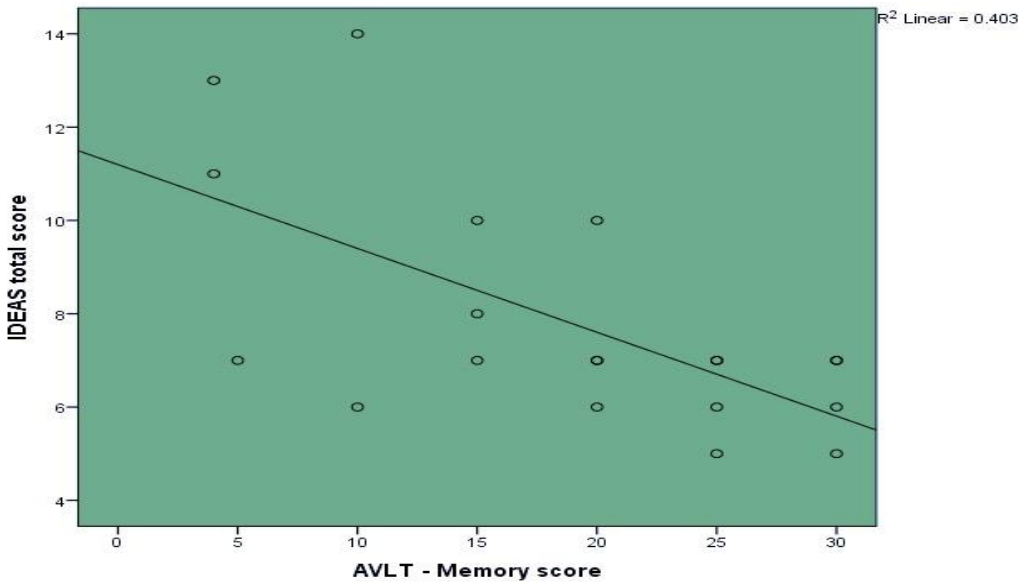


Figure 7: Relationship between AVLT-learning score and IDEAS Global score

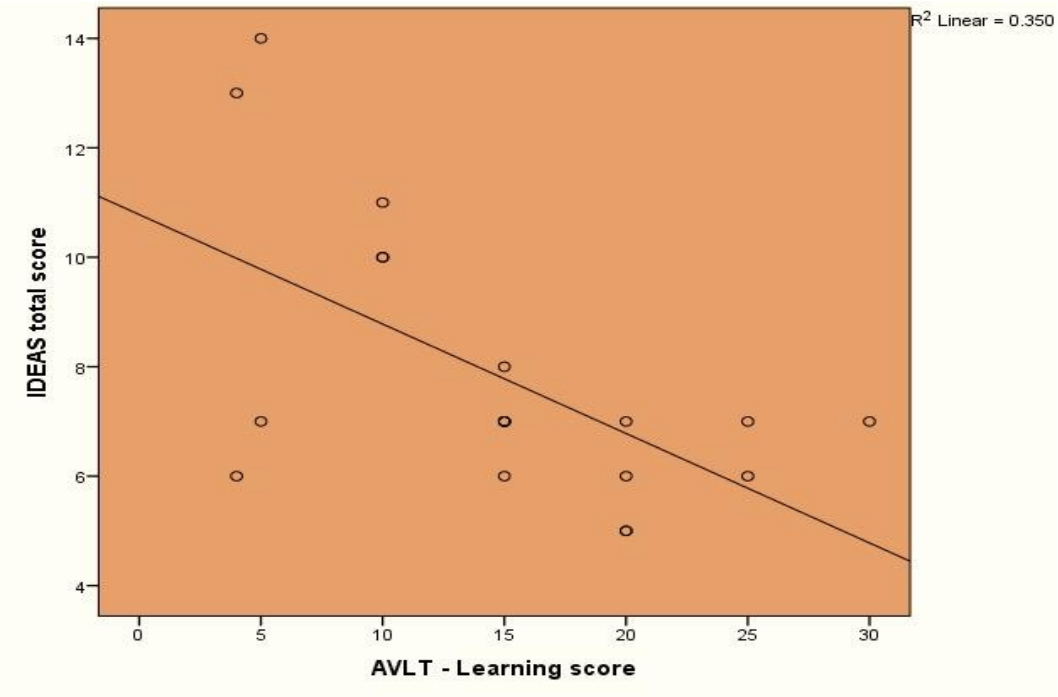


Figure 8: Relationship between AVLT-False alarms and IDEAS Global score

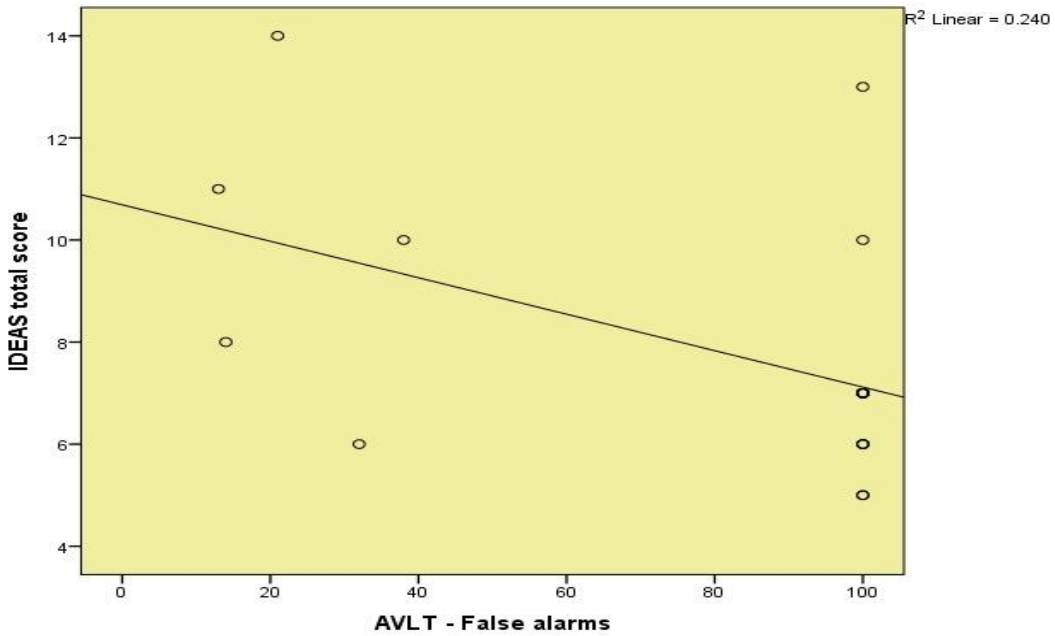
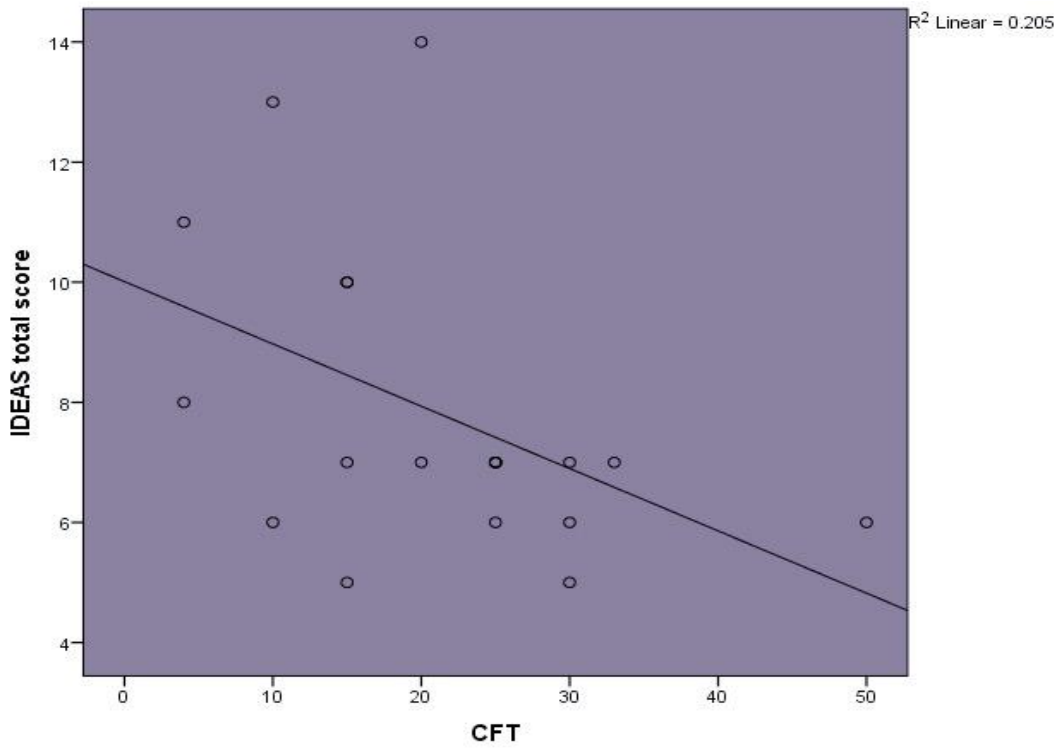


Figure 9: Relationship between CFT and IDEAS Global score



The trend line in above figures (Figures 5-9) depicts that the IDEAS Global score decreases when the scores of DST total time, AVLT memory score, AVLT learning score, AVLT false alarms and CFT increases. Thus, a negative correlation is observed between the IDEAS global score and the neuropsychological test scores that are mentioned above.

DISCUSSION

Our study aimed at finding the domains of neurocognitive deficits in clinically stable schizophrenia compared to an age and gender matched healthy control group. However, educational status is not matched in our control group. As a previous study [14] has mentioned, without having a conclusive evidence about the onset of cognitive deficits in schizophrenia that could have affected the level of education, matching for education may give spuriously low estimates of the intellectual ability of the schizophrenia patients. Using validates Indian tools, we analyzed both the neurocognitive deficits and disability in Indian population. The findings from the study are as follows.

NEUROCOGNITIVE DEFICITS IN SCHIZOPHRENIA

Our study found that, on comparing with control group, patients with Schizophrenia have deficits in all the assessed domains, such as attention, processing speed, executive functions (fluency, working memory and response inhibition), verbal learning and memory, visual-spatial construction and visual memory. This is similar to the findings from the previous studies done in the same area.[14,17] A similar study done in Indian population assessing attention, executive function, verbal and visual learning & memory using neuropsychological tests developed in other cultures, also showed a similar profile of cognitive impairments. [39]

When sub-group analyses were done in our study based on gender and education, the results did not differ much, showing statistically significant deficits in all neurocognitive domains among the schizophrenia patients. One interesting finding in our study is that, when sub-group analyses was done among males (schizophrenia Vs controls), although the mean scores were higher in the male control group, it failed to show statistically significant difference between the two groups in working memory task (Verbal N back test). This is in contrary to the previous studies which showed that, irrespective of gender, all neurocognitive domains were impaired in Schizophrenia. [30,53] A previous study done by Malaspina et al., showed that males are seen to have slightly better working memory than females. [59] One explanation is that, because males have a better working memory function innately, we did not see significant deficits when compared with healthy male controls.

Another finding from sub-group analysis is that, among participants with school-level education, the control group scored higher than schizophrenia patients on working memory testing, but this was not statistically significant. Although this is contrary to the majority of the studies showing poor premorbid level of education is a predictor of poor performance on neurocognitive tests[7,26,30], it could be explained by the concept that neurocognitive deficits in schizophrenia fall on a continuum (Heinrichs and Zakzanis, 1998). That is, there may be an overlap between schizophrenia patients with mild cognitive deficits (in our study, mild deficit in working memory) and healthy controls.

Thus, we can safely conclude that those with schizophrenia has impaired neurocognitive functioning in all the domains that were assessed.

NEUROCOGNITION & DURATION OF ILLNESS

In the clinically stable Schizophrenia group, it was found that patients with duration of illness more than 2 years have more deficits in speed of processing, verbal learning and memory, visual memory and visuo-spatial construction. Previously, various prospective and cross-sectional studies[6.8.13.17] have shown that the cognitive deficits in schizophrenia appear to stabilize over time i.e., no worsening of cognitive deficits with increasing duration of illness. Similar results were given by a large-scale meta-analysis done in 2013 which found no significant relationship between neurocognitive deficits and duration of illness.[2] Our study found that, in some of the neurocognitive domains, there were more deficits in patients with longer duration of illness, whereas some of the domains appear to have improved with longer duration of illness.

Many studies have showed that verbal learning and memory is the most consistent deficit which is seen to decline with longer duration of illness. A prospective study by Haring et al., observed that verbal learning and memory and visuo-spatial recognition declined with time.[7] This is similar to the finding from our study, which showed that patients with duration of illness more than 2 years, have significantly more deficits in verbal learning & memory and visuo-spatial construction and visual memory.

Our study also reported more deficits in processing speed among patients with longer duration of illness. Gonzalez-Ortega et al., in a 5 year follow-up study found that, no improvement in processing speed was observed over time, although most of the other neurocognitive domains appeared to have improved. Majority of the studies have found that the neurocognitive deficits become stable with time, but some studies have even showed that processing speed have improved over time, [4,7] which is contrary to our study results. We could not find an explanation for this contradicting result in our study.

Haring et al., in his prospective study, found that executive function and working memory improves with time.Similar results have been seen in other studies, that executive function and working memory improves as the duration of illness increases. [6,47] In our study, among the schizophrenia patients, those with more than 2 years of illness i.e., longer duration of illness showed higher scores on working memory and execution function (response inhibition and fluency) tests than those with duration of illness less than 2 years. But, this difference was not statistically significant.

Hence, we conclude that, the stability of neurocognitive deficits in schizophrenia still needs to be explored further.

NEUROCOGNITION AND SOCIODEMOGRAPHIC FACTORS

Owing to the differences in the neurobiology of the male and female brain, gender differences are theoretically expected in age of onset, clinical symptomatology, treatment response and prognosis in schizophrenia. A large cohort study done by Goldberg and James et al., did not find any significant difference in the performances of males and females on all neurocognitive tests. [56] In our study, among the patients with Schizophrenia, when sub-group analysis was done based on age, we found that there is no statistically difference between the scores of male and female schizophrenics on all neurocognitive tests. Both the genders have a similar profile of neurocognitive impairment. But, this is in contrary to the findings from few other studies which showed that females had a better performance than males in learning & memory, processing speed and executive function, thereby predicting a poorer outcome in males.[2,7,30] Thus, gender differences in neurocognition among schizophrenia patients still remains controversial and needs to be explored in further research. [57]

Previous studies with a similar study design have found that, the neurocognitive functioning seem to decline with age i.e., as age increased, the deficits in domains such as

processing speed and memory become more.[30] An Indian study showed similar results that memory and attention decline with increasing age. [53] Our study results revealed that although there is a decline in verbal learning in memory scores, those in the age group of 51-65 years showed a higher score than those in the age group of 31-

50 years, which was also found to be statistically significant. The same trend was observed in various other domains such as processing speed, working memory, visual memory and visuo-spatial reconstruction, those differences were not statistically significant. This finding from our study can be explained by the number of patients in each age group, with the least (only 2) in the 51-65 age group (against 9 participants in the other 2 age groups). Thus, future studies should take this into account and have a comparable number of participants in each age group.

Some of the studies done previously, have found a significant correlation between education and cognitive functioning in Schizophrenia patients. They have found that a better educational status is associated with a better cognitive performances.[7,26,53] Our study also showed similar results that, in majority of the cognitive domains assessed, college-level educated participants scored higher than those with school-level education. Though, statistically significant difference was noted only for fluency task, which is an executive function. That is, college-level educated schizophrenia patients scored significantly higher on executive function domain. But, this has not always been the case. Studies have also showed that has no significant correlation with neurocognitive functioning, and this is especially true in the normal controls.[26] Hence, even though studies have found an association, we have no conclusive evidence about the directionality of this relationship. It could be, either, that Schizophrenics with a premorbid better cognition are able to reach a higher educational status and thus have a better cognitive performance even after the onset of schizophrenia or that people with premorbid lower level of education are susceptible for poorer cognitive functioning following the onset of schizophrenia. As of now, we

don't have evidence to conclusively say that education is a protective factor for cognitive deficits in Schizophrenia.

DISABILITY & NEUROCOGNITION IN SCHIZOPHRENIA

Functional outcome is an important area of interest in Schizophrenia for many researchers. The studies that have been done so far have established a clear correlation between cognitive deficits and poor functional outcome in domains such as self-care, community participation, interpersonal relations independent living skills and work skills.[4,1518] Studies have also found an association between negative symptoms and cognitive deficits, especially verbal learning and memory impairment.[4,13,53] Based on this, a model has been hypothesized that, negative symptoms mediates the negative correlation between neurocognition and functional competence in Schizophrenia. [15]

We assessed the functional outcome of schizophrenia patients in terms of disability using IDEAS scale, which is developed specially for the Indian population. Our study found that, there is a negative correlation between disability among schizophrenia patients (based on the global score on IDEAS scale) and neurocognitive functioning, which is similar to the findings from the earlier studies. Among the neurocognitive domains, processing speed, verbal learning and memory, visual memory and visuo-spatial construction are found to have statistically significant negative correlation with disability. Previous studies[4,32,42] have also showed that, among the domains of neurocognition, processing speed, attention, verbal learning and memory and visuo-spatial constructional ability were necessary for real-world functional competence.

When correlation with each domain of the disability scale – self-care, interpersonal activities, communication and understanding and work, was analyzed, we found that processing speed and disability in work was significantly correlated in a negative manner i.e., more the deficits in processing speed, more is the disability in work domain. This finding is similar to the results from the previous studies.[18,32] It was noted that, when domains of functioning are individually analyzed for correlation with deficits in each neurocognitive domain, only processing speed was found to be significantly correlated, but not verbal learning and memory, visual memory and visuo-spatial construction which were significantly correlated with the global disability scores, as discussed earlier. One explanation for this loss of significance on breaking down the global disability score into its component scores, could be that, the global score includes an additional score for duration of illness and upon removal of which, the statistical significance for verbal learning and memory & visual memory is lost. Thereby, it again adds evidence to the earlier described result of verbal learning and memory, visual memory and visuo-spatial construction being significantly associated with duration of illness in schizophrenia.

Thus, we found that few domains of neurocognition have a significant relationship with the functional outcome in schizophrenia. Improving these specific domains of neurocognitive deficits may improve the functional outcome and thereby, quality of life of schizophrenia patients

DISABILITY AND OTHER FACTORS

When factors such as age, gender and education are analyzed for its association with disability, we found that, disability score has a significant association with increasing age. i.e., the disability is observed to be more in older age group, thereby predicting a poorer functional outcome with increasing age. Some previous studies[30,53] have suggested that, there is worsening of some neurocognitive deficits with ageing, and the relationship between disability and cognitive functioning is well-established from our study and various other studies. This could be a reason for worsening of disability with age found in our study.

When disability among males and females were compared, our study found that males have higher disability than females, although it was not statistically significant. This is similar to the results from the previous studies which reported that males have poorer functional outcomes compared to females.[2,7,30] Few other studies have reported that, owing to the better psychosocial functioning among males, males have a better functional outcome than females with schizophrenia. Thus, gender differences in functional outcome still remains controversial.

Based on level of education, we found that, school-level educated schizophrenia patients have significantly higher disability than college-level educated schizophrenics. Even though, previous studies have showed that, better premorbid level of education is a predictor of better outcome in

schizophrenia, contradicting results suggesting no relationship between education and functional outcome have also been observed. Hence, the relationship between education and functional outcome still needs to be explored.

Similar to the controversial association of neurocognitive deficits and sociodemographic variables, the association between functional outcome and sociodemographic variables are also equally controversial. Further research is needed to come to a conclusion regarding these associations.

STRENGTHS

1. We studied the cognitive functioning of patients with clinically stable schizophrenia and compared it with that of a healthy control group, thereby enabling us to analyze the differences in performance between those with schizophrenia and the normal population.

2. Our study included a control group that is age and gender matched with the schizophrenia patients, thus enabling a better comparison between the neurocognition in healthy people and those with schizophrenia.

3. Our study was done in patients with clinically stable schizophrenia where we assessed the remission by using a standardized scale i.e., PANSS and a standardized criterion for remission (given by Nancy Andreasen).

4. Among the participants with schizophrenia, we divided them into 2 groups as those with duration of illness less than 2 years and those with duration of illness more than 2 years. Thus, we were able to analyze the differences in the domains of deficits in relation to the duration of illness.

5. We used the NIMHANS Neuropsychological Battery, a validated assessment tool developed in the Indian context with normative data for the Indian population.

6. We used a Disability assessment scale which is specifically used for the Indian population, thereby eliminating the cultural variations which may potentially influence the results.

7. We correlated the functional outcome and neurocognitive deficits by analyzing the relationship between disability in each domain of functioning with the domains of cognitive impairment.

8. We explored the relationship between functional outcome and duration of schizophrenia by comparing the disability in those with duration of illness less than 2 years and those with duration of illness more than 2 years.

LIMITATIONS

In our study, we had some limitations that are worthwhile to be mentioned.

1. The sample size for our study was small which could have influenced the results and limits the generalizability of our findings. Similar studies with a larger sample size can be more beneficial to bring a better understanding about the impairments of the schizophrenia patients.

2. We used a convenient sampling method which could have led to selection bias, thereby affecting the results of the study. A consecutive sampling method or stratified sampling method may be used in future studies.

3. Blinding of the assessor was not done that could have led to potential bias in the scoring of the neuropsychological assessment.

4. Among the neurocognitive domains that are proposed to be important in schizophrenia, our study did not analyze the domains of reasoning & problem solving and social cognition.

CONCLUSION

Our study in the Indian population found that there is significant amount of impairments in neurocognition among schizophrenia patients and some of these impairments appear to worsen over time. We also found that the functional outcome of schizophrenia largely depends on few of the domains of cognitive deficits seen in these patients. Cognitive retraining for these specific cognitive deficits, given early in the course of illness may improve the functional outcome in schizophrenia patients and thereby patients with schizophrenia may no longer be considered as “life-long disabled”. Pharmacological and non-pharmacological treatment strategies for improving neurocognitive impairments is the need of the hour.

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Study Volunteer ID:
Study Volunteer Name:

PSG Institute of Medical Science and Research, Coimbatore
Institutional Human Ethics Committee
INFORMED CONSENT FORMAT FOR RESEARCH PROJECTS

(strike off items that are not applicable)

I , Dr. Sheerin Fathima carrying out a study on the topic: "Neurocognition and disability in patients with Schizophrenia compared with healthy controls" as part of my / our research project being carried out under the aegis of the Department of: Psychiatry

(*Applicable to students only*): My research guide is: Dr I Anand

The objectives of this study are:

Primary Objective: The aim of the study is to assess the neurocognitive functions among patients with clinically stable Schizophrenia and compare with healthy controls.

Secondary Objective: To compare the neurocognitive functions in clinically stable Schizophrenia patients with illness duration of less than 2 years and more than 2 years.
To correlate the degree of disability with neurocognitive functions comparing schizophrenia patients and healthy controls.

Sample size: ___50 schizophrenia patients and 50 healthy controls___.

Study volunteers / participants are (specify population group & age group): >18 – 60 years
Location: PSGIMSR, Coimbatore

We request you to kindly cooperate with us in this study. We propose collect background information and other relevant details related to this study. We will be carrying out:

Initial interview (specify approximate duration):___60___ minutes.

Data collected will be stored for a period of _NA_ years. We will / will not use the data as part of another study.

Health education sessions: Number of sessions: _____NA_____. Approximate **duration** of each session:

_____NA_____ minutes.

Clinical examination (Specify details and purpose): NA

Blood sample collection: Specify quantity of blood being drawn: _____NA_____ml.

No. of times it will be collected: _____NA_____.

Whether blood sample collection is part of routine procedure or for research (study) purpose: NA

1. Routine procedure 2. Research purpose

Specify **purpose**, discomfort likely to be felt and side effects, if any: _____NA_____

Whether blood sample collected will be stored after study period: NA

Whether blood sample collected will be sold: NA

Whether blood sample collected will be shared with persons from another institution: NA

Medication given, if any, duration, side effects, purpose, benefits: NA

Whether medication given is part of routine procedure:NA

Final interview (specify approximate duration):_____NA__ mts. If **photograph** is taken, purpose: NA

Benefits from this study: NA

Risks involved by participating in this study: NA

How the **results** will be used:

If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only. You will be informed about any significant new findings - including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date: Witness:

Contact number of PI: +91 9486170816

Contact number of Ethics Committee Office: 0422 4345818

பூ சா கோ மருத்துவக் கல்லூரி மற்றும் ஆராய்ச்சி நிறுவனம், கோவை

மனித நெறிமுறைக் குழு

ஒப்புதல் படிவம்

தேதி:

டாக்டர். அ. ஷீரின் பாத்திமா ஆகிய நான். பூ சா கோ மருத்துவக் கல்லூரியின் / மருத்துவ மனையின் மனநல மருத்துவத் துறையின் கீழ் ‘‘மனச்சிதைவு நோயாளிகளின் நரம்பியல் புலனுணர்வு செயல்பாடு மற்றும் செயல்திறன் – ஓர் ஒப்பீடு”___என்ற தலைப்பில் ஆய்வு மேற்கொள்ள உள்ளேன்.

என் ஆய்வு வழிகாட்டி (மாணவர்களுக்கு மட்டும்) : டாக்டர். ஆனந்த். ஐ

ஆய்வு மேற்கொள்வதன் அடிப்படை

மனச்சிதைவு நோயாளிகளின் நரம்பியல் புலனுணர்வு செயல்பாட்டில் குறைபாடுகள் வெகுவாகக் காணப்படுகின்றன. ஆகையால் இந்த ஆய்வின் மூலம் அவற்றின் தன்மை மற்றும் வேறுபாடுகளை அறிந்து கொள்ளவிருக்கிறேன்.

ஆய்வின் நோக்கம் :..

மனச்சிதைவு நோயாளிகளின் நரம்பியல் புலனுணர்வு செயல்பாடு மற்றும் செயல்திறன் பற்றி தெரிந்து கொள்ளுதல் அதன்மூலம் நோயாளிகளில் காணப்படும் குறைபாடுகளை நோயற்றவர்களோடு ஒப்பிடுதல்.

ஆய்வில் பங்கு பெறும் நபர்களின் எண்ணிக்கை: 50 நோயாளிகள்

50 நோயற்றவர்கள்

ஆய்வில் பங்கு பெறுவோர் மற்றும் வயது : >18 - 60

ஆய்வு மேற்கொள்ளும் இடம் :

பூ சா கோ மருத்துவமனை. கோயம்புத்தூர்

இந்த ஆய்வில் எங்களுடன் ஒத்துழைக்குமாறு கேட்டுக்கொள்கிறோம். நாங்கள் சில தகவல்களை இந்த ஆய்விற்காக சேகரிக்க உள்ளோம்.

ஆய்வு செய்யப்படும் முறை :

முதன்மை நேர் கானல் : 60 நிமிடங்கள்

இந்த ஆய்வில் கிடைக்கும் தகவல்கள் வருடங்கள் பாதுகாக்கப்படும் இந்த தகவல்கள் வேறு ஆய்விற்குப் பயன்படுத்தப்படும் / பயன்படுத்தப்பட மாட்டாது. **பொருந்**தாது

சுகாதாரக் கல்வி : பொருந்தாது

மருத்துவ பரிசோதனைகள் : பொருந்தாது

இரத்த மாதிரி சேகரிப்பு : பொருந்தாது

இரத்த மாதிரி எடுப்பது வழக்கமான சிகிச்சைக்காகவா அல்லது இந்த ஆய்விற்காகவா?

: பொருந்தாது

இதனால் ஏற்படக் கூடிய அசௌகரியங்கள் பக்க விளைவுகள் : பொருந்தாது

இரத்த மாதிரிகள் ஆய்விற்குப் பின் பாதுகாத்து வைக்கப்படுமா? : பொருந்தாது

சேகரிக்கப்பட்ட இரத்தம் வேறு நிறுவனத்துடன் பகிர்ந்து கொள்ளப்படுமா? : பொருந்தாது

மருந்துகள் ஏதேனும் கொடுக்கப்படவிருந்தால் அவை பற்றிய விவரம் (கொடுக்கப்படும் காரணம், பக்க வளைவுகள் பயன்கள்) : பொருந்தாது

மருந்துகள் கொடுக்கப்படுவது வழக்கமான சிகிச்சை முறையா? : பொருந்தாது

கொடுக்கப்படும் மருந்துகளுக்கு மாற்று உள்ளதா? : பொருந்தாது

ஆய்வில் பங்கு பெறுவதால் ஏற்படும் பலன்கள் **: பொருந்**தாது

ஆய்வில் பங்கேற்பதால் ஏற்படும் அசௌகரியங்கள் பக்க விளைவுகள் : பொருந்தாது

ஆய்வின் முடிவுகள் எந்த முறையில் பயன்படுத்தப்படும்?

ஆய்வுக்குட்படுபவரின் ஒப்புதல் :

நான் இந்த ஆராய்ச்சியின் நோக்கம் மற்றும் அதன் பயன்பாட்டினைப் பற்றி தெளிவாகவும். விளக்கமாகவும் தெரியப்படுத்தப்படடுள்ளேன். இந்த ஆராய்ச்சியில் பங்கு கொள்ளவும். இந்த ஆராய்ச்சியின் மருக்துவ ரீதியான குறிப்புகளை வரும் காலத்திலும் உபயோகப்படுத்திக் கொள்ளவும் முழு மனதுடன் சம்மதிக்கிறேன்.

ஆய்வுக்குட்படுபவரின் பெயர். முகவரி :
தேதி :

ஆய்வாளரின் கையொப்பம் :
தேதி :

ஆய்வாளரின் தொலைபேசி எண் : 9486170816

நெறிமுறை குழு அலுவலக தொலைபேசி எண் : 0422 – 2570170 உள்தொடர்பு எண் : 5818

PANSS RATING FORM

		absent	minimal	mild	moderate	moderate severe	severe	extreme
P1	Delusions	1	2	3	4	5	6	7
P2	Conceptual disorganisation	1	2	3	4	5	6	7
P3	Hallucinatory behaviour	1	2	3	4	5	6	7
P4	Excitement	1	2	3	4	5	6	7
P5	Grandiosity	1	2	3	4	5	6	7
P6	Suspiciousness/persecution	1	2	3	4	5	6	7
P7	Hostility	1	2	3	4	5	6	7
N1	Blunted affect	1	2	3	4	5	6	7
N2	Emotional withdrawal	1	2	3	4	5	6	7
N3	Poor rapport	1	2	3	4	5	6	7
N4	Passive/apathetic social withdrawal	1	2	3	4	5	6	7
N5	Difficulty in abstract thinking	1	2	3	4	5	6	7
N6	Lack of spontaneity & flow of conversation	1	2	3	4	5	6	7
N7	Stereotyped thinking	1	2	3	4	5	6	7
G1	Somatic concern	1	2	3	4	5	6	7
G2	Anxiety	1	2	3	4	5	6	7
G3	Guilt feelings	1	2	3	4	5	6	7
G4	Tension	1	2	3	4	5	6	7
G5	Mannerisms & posturing	1	2	3	4	5	6	7
G6	Depression	1	2	3	4	5	6	7
G7	Motor retardation	1	2	3	4	5	6	7
G8	Uncooperativeness	1	2	3	4	5	6	7
G9	Unusual thought content	1	2	3	4	5	6	7
G10	Disorientation	1	2	3	4	5	6	7
G11	Poor attention	1	2	3	4	5	6	7
G12	Lack of judgement & insight	1	2	3	4	5	6	7
G13	Disturbance of volition	1	2	3	4	5	6	7
G14	Poor impulse control	1	2	3	4	5	6	7
G15	Preoccupation	1	2	3	4	5	6	7
G16	Active social avoidance	1	2	3	4	5	6	7

Patient Name:		***Patient Number:***	
Date of Birth:		***Time Interview Began:***	
Interviewer's Name:		***Time Interview Ended:***	
Date of Interview:		***Total Time:***	

	MODULES	TIME FRAME	MEETS CRITERIA	DSM-IV	ICD-10	
A	MAJOR DEPRESSIVE EPISODE	Current (2 weeks)	☐	296.20-296.26 Single	F32.x	❐
		Recurrent	☐	296.30-296.36 Recurrent	F33.x	❐
	MDE WITH MELANCHOLIC FEATURES	Current (2 weeks)	☐	296.20-296.26 Single	F32.x	❐
	Optional			296.30-296.36 Recurrent	F33.x	❐
B	DYSTHYMIA	Current (Past 2 years)	☐	300.4	F34.1	❐
C	SUICIDALITY	Current (Past Month) Risk: ☐ Low ☐ Medium ☐ High	☐			❐
D	MANIC EPISODE	Current	☐	296.00-296.06	F30.x-F31.9	❐
		Past	☐			
	HYPOMANIC EPISODE	Current	☐	296.80-296.89	F31.8-F31.9/F34.0	❐
		Past	☐			
E	PANIC DISORDER	Current (Past Month)	☐	300.01/300.21	F40.01-F41.0	❐
		Lifetime	☐			
F	AGORAPHOBIA	Current	☐	300.22	F40.00	❐
G	SOCIAL PHOBIA (Social Anxiety Disorder)	Current (Past Month)	☐	300.23	F40.1	❐
H	OBSESSIVE-COMPULSIVE DISORDER	Current (Past Month)	☐	300.3	F42.8	❐
I	POSTTRAUMATIC STRESS DISORDER	Current (Past Month)	☐	309.81	F43.1	❐
J	ALCOHOL DEPENDENCE	Past 12 Months	☐	303.9	F10.2x	❐
	ALCOHOL ABUSE	Past 12 Months	☐	305.00	F10.1	❐
K	SUBSTANCE DEPENDENCE (Non-alcohol)	Past 12 Months	☐	304.00-.90/305.20-.90	F11.1-F19.1	❐
	SUBSTANCE ABUSE (Non-alcohol)	Past 12 Months	☐	304.00-.90/305.20-.90	F11.1-F19.1	❐
L	PSYCHOTIC DISORDERS	Lifetime	☐	295.10-295.90/297.1/	F20.xx-F29	❐
		Current	☐	297.3/293.81/293.82/ 293.89/298.8/298.9		
	MOOD DISORDER WITH PSYCHOTIC FEATURES	Lifetime	☐	296.24/296.34/296.44	F32.3/F33.3/ ❐	
		Current	☐	296.24/296.34/296.44	F30.2/F31.2/F31.5 F31.8/F31.9/F39 ❐	
M	ANOREXIA NERVOSA	Current (Past 3 Months)	☐	307.1	F50.0	❐
N	BULIMIA NERVOSA	Current (Past 3 Months)	☐	307.51	F50.2	❐
	ANOREXIA NERVOSA, BINGE EATING/PURGING TYPE	Current	☐	307.1	F50.0	❐

O	GENERALIZED ANXIETY DISORDER	Current (Past 6 Months)	☐	300.02	F41.1	❐
P	ANTISOCIAL PERSONALITY DISORDER Optional	Lifetime	☐	301.7	F60.2	❐

Which problem troubles you the most? Indicate your response by checking the appropriate check box(es).

NEUROCOGNITION AND DISABILITY IN PATIENTS WITH SCHIZOPHRENIA COMPARED WITH HEALTHY CONTROLS

PATIENT PROFORMA

Name

Age

Sex

Marital status

Educational status

Occupation

Duration of illness

Number of hospitalisation

Duration of treatment

Treatment details

PANSS score

IDEAS disability percentage score

S.No	TESTS	PERCENTILE SCORE		PERCENTILE SCORE	
1	Digit symbol substitution	TT			
2	Digit vigilance	TT		ERRORS	
3	COWA	ANW			
4	Animal naming	TNW			
5	Verbal N back	HITS		ERRORS	
6	Stroop test	SE			
7	Auditory verbal learning test	MS		MISSES	
				FALSE ALARM	
8	Comlpex figure test				

IDEAS SCORING SHEET

ITEMS	**0**	**1**	**2**	**3**	**4**
SELF CARE					
INTERPERSONAL ACTIVITIES					
COMMUNICATION & INTERACTION					
WORK					
TOTAL SCORE					
DOI SCORE					
GLOBAL SCORE					

DIGIT SYMBOL SUBSTITUTION TEST

1	2	3	4	5	6	7	8	9
—	⊥	⌝	L	U	O	Λ	X	=

2	1	3	7	2	4	8	1	5	4	2	1	3	2	1	4	2	3	5	2	3	1	4	6	3

1	5	4	2	7	6	3	5	7	2	8	5	4	6	3	7	2	8	1	9	5	8	4	7	3

6	2	5	1	9	2	8	3	7	4	6	5	9	4	8	3	7	2	6	1	5	4	6	3	7

9	2	8	1	7	9	4	6	8	5	9	7	1	8	5	2	9	4	8	6	3	7	9	8	6

DVT

9 5 3 6 4 7 2 8 1 9 2 8 6 2 4 1 2 4 6 8 9 7 3 5 1 8 5 4 2 9
8 4 2 1 3 5 6 1 9 7 5 6 3 8 2 3 9 7 4 1 2 3 4 5 6 7 8 9 1 2
1 7 4 8 6 3 2 9 7 1 4 3 2 5 9 5 7 8 6 3 4 5 6 1 7 2 8 3 9 4
6 1 3 2 9 4 6 5 8 7 3 1 9 5 1 7 5 9 8 1 7 2 8 3 9 4 1 5 2 6
4 6 7 1 5 3 2 9 1 8 6 4 2 8 6 9 3 1 5 3 1 4 2 5 3 6 4 7 5 8
2 3 8 2 6 9 7 4 9 1 3 8 6 9 2 2 1 3 8 6 3 7 4 8 5 9 6 1 7 2
5 8 9 3 1 7 2 6 8 4 1 3 5 7 9 4 8 2 9 4 8 5 9 6 1 7 2 8 3 9
3 9 1 4 2 6 8 7 5 1 3 2 4 6 8 6 6 4 1 1 8 5 2 9 6 3 1 7 4 2
6 2 3 5 7 9 1 4 8 2 4 1 3 7 9 8 2 5 2 9 3 1 7 4 2 5 7 6 3 5
9 2 5 6 1 3 7 2 4 6 1 7 8 3 5 9 4 6 3 1 8 5 2 9 6 3 1 4 2 7
8 3 7 8 2 6 4 9 1 5 7 2 4 6 8 7 9 8 4 6 9 1 4 7 1 2 5 8 4 3
7 4 9 7 1 3 5 2 4 6 9 8 1 3 7 5 7 9 6 1 6 3 8 4 9 5 1 6 2 7
4 5 2 9 2 1 3 7 9 8 2 6 2 4 1 3 5 7 8 3 7 8 3 9 4 1 5 2 6 7
2 6 4 1 9 4 3 5 7 1 4 7 3 1 4 1 3 9 5 7 8 1 6 2 7 3 8 4 9 5
5 7 6 3 1 9 6 5 6 3 5 8 6 2 5 8 1 7 9 5 9 2 4 6 8 1 3 5 7 9
3 8 2 5 6 4 2 8 7 2 6 9 7 3 8 6 2 8 7 9 1 2 3 5 3 9 1 7 3 4
2 9 8 7 1 3 5 7 9 8 4 2 6 9 7 4 8 6 1 2 3 4 5 7 8 4 6 2 8 9
1 7 4 9 5 6 8 3 2 1 3 5 7 8 2 2 6 5 3 4 2 6 7 9 4 1 2 8 4 5
6 5 8 2 1 3 9 7 4 9 7 5 3 1 8 5 4 3 2 6 4 8 9 2 9 5 7 3 9 1
4 6 3 4 9 2 5 8 2 5 2 8 5 2 3 3 1 4 5 8 5 1 2 4 5 2 3 9 5 6
5 4 5 6 8 1 4 7 1 6 3 9 6 4 5 7 2 1 4 1 6 3 4 6 1 6 8 4 1 2
3 2 7 8 6 9 3 6 1 7 4 1 7 6 7 9 3 2 6 2 7 5 6 8 6 3 4 1 6 7
1 3 9 5 4 8 2 5 2 8 5 2 8 8 9 4 5 1 7 3 8 7 8 1 2 7 9 5 2 3
9 1 8 3 5 7 1 4 3 9 6 3 9 1 2 6 4 2 8 4 1 9 1 2 7 4 5 2 7 8
6 4 2 9 3 6 9 3 4 1 7 4 1 3 4 2 6 3 9 5 2 1 3 4 3 8 1 6 3 4
9 5 3 6 4 7 2 8 1 9 2 8 6 2 4 1 2 4 6 8 9 7 3 5 1 8 6 4 2 9
8 4 2 1 3 5 6 1 9 7 5 6 3 8 2 3 9 7 4 1 2 3 4 5 6 7 8 9 1 2
1 7 4 8 6 3 2 9 7 1 4 3 2 5 9 5 7 8 6 3 4 5 6 1 7 2 8 3 9 4
6 1 3 2 9 4 6 5 8 7 3 1 9 5 1 7 5 9 8 1 7 2 8 3 9 4 1 5 2 6
4 6 7 1 5 3 2 9 1 8 6 4 2 8 6 9 3 1 5 3 1 4 2 5 3 6 4 7 5 8
2 3 8 2 6 9 7 4 9 1 3 8 6 9 2 2 1 3 8 6 3 7 4 8 5 9 6 1 7 2
5 8 9 3 1 7 2 6 8 4 1 3 5 7 9 4 8 2 9 4 8 5 9 6 1 7 2 8 3 9
3 9 1 4 2 6 8 7 5 1 3 2 4 6 8 6 6 4 1 1 8 5 2 9 6 3 1 7 4 2
6 2 3 5 7 9 1 4 8 2 4 1 3 7 9 8 2 5 2 9 3 1 7 4 2 5 7 6 3 5
9 2 5 6 1 3 7 2 4 6 1 7 8 3 5 9 4 6 3 1 8 5 2 9 6 3 1 4 2 7
8 3 7 8 2 6 4 9 1 5 7 2 4 6 8 7 9 8 4 6 9 1 4 7 1 2 5 8 4 3
7 4 9 7 1 3 5 2 4 6 9 8 1 3 7 5 7 9 6 1 6 3 8 4 9 5 1 6 2 7
4 5 2 9 2 1 3 7 9 8 2 6 2 4 1 3 5 7 8 3 7 8 3 9 4 1 5 2 6 7
2 6 4 1 9 4 3 5 7 1 4 7 3 1 4 1 3 9 5 7 8 1 6 2 7 3 8 4 9 5
5 7 6 3 1 9 6 5 6 3 5 8 6 2 5 8 1 7 9 5 9 2 4 6 8 1 3 5 7 9
3 8 2 5 6 4 2 8 7 2 6 9 7 3 8 6 2 8 7 9 1 2 3 5 3 9 1 7 3 4
2 9 8 7 1 3 5 7 9 8 4 2 6 9 7 4 8 6 1 2 3 4 5 7 8 4 6 2 8 9
1 7 4 9 5 6 8 3 2 1 3 5 7 8 2 2 6 5 3 4 2 6 7 9 4 1 2 8 4 5

Time taken: Errors: S_____
O_____

AUDITORY – VERBAL LEARNING TEST

English Version

S.No.	LIST-A	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	**LIST B**		IR-A	DR-A	Recognition
1	Arm						Shoes				**Hits**
2	Cat						Monkey				Mirror
3	Axe						Bowl				**Hammer**
4	Bed						Cow				**Knife**
5	Plane						Finger				Candle
6	Ear						Dress				Motorcycle
7	Dog						Spider				**Axe**
8	Hammer						Cup				**Clock**
9	Chair						Bee				**Chair**
10	Car						Foot				**Plane**
11	Eye						Hat				Turtle
12	Horse						Butterfly				Leg
13	Knife						Kettle				**Dog**
14	Clock						Mouse				Table
15	Bike						Hand				**Cat**
											Lips
											Tree
											Arm
											Nose
											Sun
											Truck
											Eye
											Fish
											Ear
											Horse
											Bike
											Stool
											Bus
											Bed
											Car
	TOTAL										

Total Scores

Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	List B	IR-A	DR	Recognition	
								HITS	
								OMISSION	
								COMMISSION	

AUDITORY – VERBAL LEARNING TEST
Tamil Version

S.No.	LIST-A	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	**LIST B**		IR-A	DR-A	Recognition
1	Kendakai						Kaalani				**Hits**
2	Poonai						Korangu				Kannadi
3	Kodali						Kinnam				**Suthiyel**
4	Padukai						Maadu				**Kathee**
5	Vaanurthi						Viral				Melaguvarthi
6	Kathu						Aadai				Scooter
7	Nayi						Ettukalpuchi				**Kodali**
8	Suthiyel						Tumbler				**Gadikaram**
9	Narkali						Theynee				**Narkali**
10	Car						Paadham				**Vannurthi**
11	Kannu						Thopi				Aamey
12	Kudirai						Pattampuchi				Kaalu
13	kathee						Kettle				**Naayi**
14	Gadikaram						Eli				Mejai
15	Bike						Kai				**Poonai**
											Udhadu
											Maram
											Kendakai
											Mooku
											Sooryan
											Lorry
											Kannu
											Meen
											Kadhu
											Kudurai
											Bike
											Stool
											Perundhu
											Padukai
											Car
	TOTAL										

Total Scores

Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	List B	IR-A	DR	Recognition	
								HITS	
								OMISSION	
								COMMISSION	

ANIMAL NAMING TEST

Total Score:

COWA TEST

F (*ka)*	A (p*a)*	S (*ma)*
Total:	Total:	Total:
	Average no. of new words:	

STROOP TEST

Stroop effect score = Time taken to name (sec) – Time taken to read the word (C – W)

VERBAL WORKING MEMORY

1 BACK

1	GA	
2	JA	
3	**JA**	
4	CHA	
5	HA	
6	**HA**	
7	SHA	
8	RA	
9	NA	
10	MA	
11	**MA**	
12	KA	
13	PA	
14	**PA**	
15	LA	
16	VA	
17	TA	
18	**TA**	
19	LA	
20	PA	
21	VA	
22	**VA**	
23	DA	
24	**DA**	
25	CHA	
26	SHA	
27	**SHA**	
28	GA	
29	YA	
30	**YA**	

2 BACK

1	NA	
2	GA	
3	**NA**	
4	MA	
5	LA	
6	JA	
7	**LA**	
8	MA	
9	KA	
10	LA	
11	**KA**	
12	JA	
13	YA	
14	MA	
15	**YA**	
16	DHA	
17	BHA	
18	**DHA**	
19	VA	
20	SHA	
21	**VA**	
22	GA	
23	**VA**	
24	**GA**	
25	DA	
26	NA	
27	**DA**	
28	CHA	
29	RA	
30	MA	

	H	**O**	**C**	**ERROR (O+C)**
1 BACK				
2 BACK				

RED	BLUE	GREEN	RED	BLUE
GREEN	GREEN	RED	BLUE	GREEN
BLUE	RED	BLUE	GREEN	RED
GREEN	BLUE	RED	RED	BLUE
RED	RED	GREEN	BLUE	GREEN
BLUE	GREEN	BLUE	GREEN	RED
RED	BLUE	GREEN	BLUE	GREEN
BLUE	GREEN	RED	GREEN	RED
GREEN	RED	BLUE	RED	BLUE
BLUE	GREEN	GREEN	BLUE	GREEN
GREEN	RED	BLUE	RED	RED
RED	BLUE	RED	GREEN	BLUE
GREEN	RED	BLUE	RED	GREEN
BLUE	BLUE	RED	GREEN	RED
RED	GREEN	GREEN	BLUE	BLUE
BLUE	BLUE	RED	GREEN	RED
RED	GREEN	BLUE	RED	GREEN
GREEN	RED	GREEN	BLUE	BLUE
RED	BLUE	RED	GREEN	RED
GREEN	RED	GREEN	BLUE	GREEN

சிவப்பு நீலம் பச்சை சிவப்பு
நீலம்
பச்சை பச்சை சிவப்பு நீலம்
பச்சை
நீலம் சிவப்பு நீலம் பச்சை
சிவப்பு
பச்சை நீலம் சிவப்பு சிவப்பு
நீலம்
சிவப்பு சிவப்பு பச்சை நீலம்
பச்சை
நீலம் பச்சை நீலம் பச்சை
சிவப்பு
சிவப்பு நீலம் பச்சை நீலம் பச்சை
நீலம் பச்சை சிவப்பு பச்சை
சிவப்பு
பச்சை சிவப்பு நீலம் சிவப்பு
நீலம்
நீலம் பச்சை பச்சை நீலம்
பச்சை
பச்சை சிவப்பு நீலம் சிவப்பு சிவப்பு
சிவப்பு நீலம் சிவப்பு பச்சை
நீலம்
பச்சை சிவப்பு நீலம் சிவப்பு பச்சை
நீலம் நீலம் சிவப்பு பச்சை சிவப்பு
சிவப்பு பச்சை பச்சை நீலம்
நீலம்
நீலம் நீலம் சிவப்பு பச்சை சிவப்பு
சிவப்பு பச்சை நீலம் சிவப்பு
பச்சை

பச்சை சிவப்பு பச்சை நீலம்

நீலம்

சிவப்பு நீலம் சிவப்பு பச்சை சிவப்பு

பச்சை சிவப்பு பச்சை

நீலம் பச்சை